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Policy

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

Change of Address

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FRONT COVER: NAVAL DENTAL RESEARCH INSTITUTE. Although established 1 January 1967 at Great Lakes this research and development facility had its beginning in 1947 as the Dental Research Facility of the Naval Training Center's Dental Department, an agency with which the Dental Research Laboratory at Bainbridge, Md. was merged in 1959. BUMED is in command of and has primary support responsibility for the Institute, while the Commandant, 9th Naval District, provides area coordination. The NDRI's expanded mission is to conduct research, development, testing and evaluation in dental and allied sciences, with particular emphasis on dental and oral health problems in Navy and Marine Corps populations and stress on fleet and field dentistry questions. To fulfill this mission varied studies have been initiated. A single organism (streptococcus) has been isolated and found to produce caries in experimental animals. Vaccines which may prevent caries are being developed and their nature is being assayed by experimental trials in animals susceptible to caries caused by human streptococci. The Institute has continued basic scientific research designed to abate, prevent and eliminate dental caries and periodontal disease through improved therapeutics and the enhancement of natural resistance to oral disease. Research has also been devoted productively to increasing staff efficiency at treatment facilities. Computer methodologies are being adapted for use in patient scheduling, treatment planning and record keeping. In addition, a new dental operatory design for military environments has been completed, and the use of auxiliary personnel at dental care activities has been expanded. It is expected that these efforts will bring about a significant reduction in the 8,000,000 man-hours lost annually in the Naval Establishment owing to dental caries and diseases which require treatment.

The issuance of this publication approved by the Secretary of the Navy on 4 May 1964.

THE NEUROSURGICAL TREATMENT OF MISSILE WOUNDS OF THE BRAIN

CDR Frederick E. Jackson, MC USN, Naval Hospital, Camp Pendleton, California 92055.

Experience derived from the treatment of missile wounds of the brain, incurred during the recent fighting in Vietnam, and treated aboard the USS SANCTUARY, has served to underscore certain principles of treatment promulgated from prior conflicts, but has also revealed that progress during the interwar period has allowed certain new concepts and equipment to be utilized. It may be helpful at this time to list the "maxims" which I have found helpful in the treatment of this type of wound, for bullet wounds of the brain are sporadically encountered in civilian life. Many of these "maxims" are common surgical practice, and are included for re-emphasis. Others are new to this conflict, made possible by better diagnostic, surgical and pharmacologic aids in neurosurgical treatment since the last (Korean) War.

Initial Evaluation and Treatment of a Patient With a Missile Wound of the Brain

1. *Direct first attention to the airway.* If a tracheostomy is needed, insert a large (#8 or #9) cuff type tracheostomy tube with a #15 Forreger adapter. The use of a balloon-cuff tracheostomy tube obviates the necessity of changing the tube prior to surgery and allows for intermittent positive pressure breathing to be given in the postoperative period. The inflated cuff also prevents blood dripping from associated maxillo-facial wounds into the bronchioles.

2. Order adequate whole blood in the triage area. Although patients with closed head injuries are seldom in hypotensive shock, missile wounds of the brain are *often* associated with hypotensive shock. This is a result of bleeding from the wound itself or from associated wounds due to missiles elsewhere in the body. It is not unusual to see the arms, face, abdomen and pelvis penetrated by 30 or 40 fragments, and the chest may also be penetrated if the Marine has not been wearing his body armor. Even the small wounds bleed and the total hypotensive effect often seems more than additive. Hence, blood loss from many small bleeding orifices can add up and precipitate frank hypovolemic shock. Association laceration of major vessels, viscera or comminuted fractures will of course bleed massively and contribute to the blood loss. I order ten units of whole blood to be typed and crossmatched for a patient with a missile wound of the brain who has associated intraabdominal or intrathoracic fragments. To save time and multiple venipunctures, obtain a stat "H and H" at the time blood is being drawn for typing and crossmatching.

3. Use large bore intravenous plastic catheters for administration of fluids and blood. If there is any doubt about the ability to cannulate veins, then by far the best recourse is to do a rapid cutdown, using *extra large plastic intravenous catheters.* There should be no question about the positioning of the intravenous catheter. On such small details does the patients life depend. Use the upper extremities when possible to avoid subsequent thrombophlebitis.

4. After the airway is clear and shock, when present, is treated, and the intravenous is running well, *re-examine the patient very carefully.* Look at the wound and correlate it with the other wounds and the patient's condition. Try to determine the direction taken by the fragment, and what structures it most likely damaged, unless deflected. An apparent wound of the chest may carry down to the spleen. Wounds of entry in the shoulder, neck, abdomen or pelvis may end up in the chest. Brain wounds are best left unprobed until the patient is on the operating table and fully prepped and draped, as probing the brain will usually start bleeding, and if it is from sinuses or large bleeding veins, several units of blood may be lost before you are able to deal properly with it.

The opinions or assertions in this paper are those of the author and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

5. Triage the patients carefully and decide which ones must be done now, and which ones can wait until you are free. Consider the presence of associated wounds when making this decision, viz. bleeding from spleen, liver or vessels.

6. In X-ray, correlate the AP with the lateral views. What may initially appear as an intracranial fragment on the lateral view may be a fragment lying anteriorly or posteriorly on the curve of the skull and hence extracranial. Take tangential views if doubt exists. The same applies to chest and abdominal films.

Definitive Treatment

7. As the patient is being prepared for surgery, have a Foley catheter inserted and check for gross hematuria. Insert a nasogastric tube to aspirate the stomach. The entire scalp is prepared even though the wound may be unilateral, for the skin under the dressings must be as sterile as possible. Administer 0.5 cc of tetanus toxoid.

8. In surgery, after the scalp is prepared (I use Betadine), excise the jagged wound edges of the wounds of entry and exit. Use gently curved incisions when possible rather than straight lines. Avoid cutting across the branches of the facial nerve. Use concealed incisions whenever possible.

9. When planning the type of bony opening, e.g., either an osteoclastic or osteoplastic craniotomy, remember that *"adequate exposure is the key to success."*[1] Be sure the bony opening is large enough to visualize normal dura around each margin. The type of bony opening in the skull is important. In the Korean Conflict, practically all openings were osteoclastic craniectomies with the resultant skull defect being plated 6 to 12 months later in CONUS. Exceptions to this were "hidden" frontal osteoplastic flaps. With the advent of air craniotomes a small burr hole may be made away from the hole of entry in the skull (and *away* from major venous sinuses), and an osteoplastic bone flap quickly cut, affording excellent exposure.[2] The margins of the hole of entry are debrided by the drill. This allows for excellent wound exposure, repositions normal anatomy and obviates the necessity for subsequent cranioplasty. If the bone is extensively shattered, however, and osteoclastic craniectomy must be performed. Here is a point to remember—It is, at this stage of the procedure, before formal debridement has been started, with its resultant bleeding and possible dislocation of bone fragments, that 99% of the intrinsic bone fragments may be palpated and carefully removed without stirring up bleeding. A sensitive palpating finger guided by a carefully handled forceps at this stage of the debridement will save both time and blood loss. Open the dura and gently palpate for the direction of the tract and for bony fragments before the wound is disturbed. Remove by sucker all necrotic brain, bone fragments and all accessible metallic fragments.

10. Copious irrigation with normal saline will wash out small, undetected metallic or bony fragments, but be careful not to loculate the irrigating fluid subdurally under pressure, for that will cause herniation of the brain into the wound.

11. Secure all bleeding with Bovie or "Hemoclips." A hydrogen peroxide soaked patty is useful in stopping capillary oozing.[3]

12. Close the dura, either directly with 4-0 silk sutures, or with a graft of temporalis fascia or pericranium. Large dural defects may be closed with fascia lata or (when available) freeze dried reconstituted human dura from the tissue bank at the National Naval Medical Center, Bethesda, Maryland. (Available to hospital ships.)

13. When there are many extensive "bursting" fractures, with oozing from many fracture lines, I insert a Snyder "Hemovak" type drain under the scalp, extradurally for 24 hours.

14. When an osteoplastic bone flap is used for exposure, the flap may be turned rapidly by using a turbine craniotome. Attachments to this instrument may be used for the initial burr hole, and for wiring the bone flap back into place.

15. The galea is closed with 4-0 silk, and although the time honored method of closing the scalp is with interrupted silk sutures, I have obtained excellent scalp approximation with a running locked suture of 3-0 dermalon with a swaged-on needle, which is a much faster method of suturing the scalp.

16. Intravenous 30% Urea, 1.5 grams per kilogram, may be used after the brain has been adequately debrided to alleviate cerebral edema. An alternative is 10% Mannitol, 2 to 3 grams per kilogram. I usually prefer the Mannitol, although its rapidity of action is slower than that of the Urea.

17. Routine postoperative skull X-rays are obtained to ascertain the completeness of removal of bony and metallic fragments.[4] High MA, overpenetrated techniques, are used for optimum definition.

18. The echoencephalogram has been a most useful diagnostic instrument when faced with the possibility of an intracranial hematoma from a blunt head injury. Its use has not been practical, however, with

missile wounds of the brain, for the decision to operate is made on the basis of the position of the wounds of entry and exit, usually readily visible, and by the position of the intracranial fragments on the X-rays.

19. Similarly, carotid or vertebral angiography has not been used initially with missile wounds of the brain. Its greatest usefulness is with closed head injuries, or in diagnosing delayed complications of wounds of the brain.

20. The use of steroids in missile wounds of the brain has, in my experience, been a two-edged sword. There is no doubt that they predispose to stress G. I. bleeding in the postoperative period, and as such, I prefer not to use them routinely. However, if cerebral edema is massive, and the patient likely to die because of it, then the added risk of stress bleeding is assumed and steroids are administered. I use 50 mgm of Solumedrol intravenously as a stat dose, tapering the dose over the course of a week, and keeping the patient on Probanthine, 15 mgm qid and Amphogel, 30 cc qid, as soon as he is able to tolerate the latter either orally or by nasogastric tube.

21. Remember the wounding agent and plan your debridement of the brain accordingly. High velocity bullet wounds of the brain require much more extensive debridement as the absorption of energy from their relatively high velocities and mass results in a much larger area of brain necrosis. Mortar, grenade, artillery or booby trap fragments on the other hand are usually of lower velocity. Hence the surrounding brain is not as necrotic. Do not *aggrevate neurological injury by overenthusiastic debridement of a low velocity missile tract.*

22. Whenever possible, in the presence of multiple wounds, work simultaneously and not consecutively with the general surgeons, urologist or orthopedist.

23. The most common wounds overlooked by the neophyte are those of the back and of the occiput. It is sobering fact that extremely large wounds of the back of the head, concealed within matted hair, may be completely overlooked unless carefully examined for by palpation and inspection. Similarly, wounds of the back are missed unless the patient is rolled on his side and his backside inspected.

24. Ninety percent of all oriented patients who are not aphasic will be able to tell you the wounding agent, e.g. bullet, mortar, rocket, artillery or booby trap. With patients who do not know, or cannot tell you the type of wounding agent, it may be surmised by a careful study of the preoperative X-rays. Intracranial mortar and artillery fragments tend to be larger, are less likely to cause tangential injuries as they are often deflected from a tangential course by the helmet, and therefore penetrate the skull at more or less right angles. The fragments may be single or in clusters. The smaller fragments, circa 1 mm in size, do not usually have the mass to penetrate the skull, although they may lodge in the skin, muscle or bone, unless the bone involved is the squamous portion of the temporal bone, in which case even small fragments will penetrate. The patient is usually not as severely wounded with either mortar or artillery fragments, unless they are massive or multiple wounds, as the absorption of energy is much less than with rifle bullets.

25. Patients with wounds due to rifle bullets, on the other hand, who survive to reach medical aid, usually present with tangential wounds. Through and through rifle bullet wounds of the brain, or traversing both hemispheres, are generally fatal. Pistol bullet wounds, however, presumably due to their lower velocity, may survive although they are complete "through and through wounds." Small, jagged bits of metal from the helmet and from the jacket of the bullet, peel off with tangential bullet wounds and are identified along with the bullet itself, or portions thereof. These small peelings are generally more jagged and irregular than mortar and artillery fragments and are more likely to be curved or bent. The amount of bone that can be indriven by tangential rifle bullet wounds is astounding. Large fragments of bone are often driven completely through a hemisphere. The degree of brain necrosis following surrounding rifle bullet tracts is more extensive than that of mortar fragments or even pistol wounds, and hence a *wider debridement is necessary.* The dura is often blown away, necessitating a dural graft. Large areas of skull are shattered, so the craniectomy required is larger than that required of mortar and artillery wounds. One thousand cc of 10% Mannitol daily for three postoperative days has proved helpful in the general management of the associated cerebral edema, even following adequate resection of the necrotic or swollen brain. The clinical course of patients who receive Mannitol seems to have been smoother than in those to whom it was not administered.

In summary, improved cuff tracheostomy tubes, plastic intravenous cannulae, availability of fresh whole blood, rapidly processed X-rays, echoencephalography, cerebral angiography, automatic drills, pneumatic craniotomes, freeze dried dura, newer antibiotics, improved neurosurgical clips and suture

materials and osmotic diuretics have all contributed to improve the rapidity and finesse with which missile wounds of the brain may be diagnosed and treated. More important, however, are the niceties of surgical judgment that must be exercised when presented with a patient or patients with these wounds, including decisions on the proper triage of patients, the assessment of associated wounds, planning the correct approach and, very important, the radicalness of resection of damaged brain. To the receptive mind, these subtleties in judgment may be developed only through experience, either personal or through perusal of others' experiences and conclusions. It is for this reason that these suggestions for the management of patients with brain injuries due to missiles are submitted.

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COCCIDIOIDES AS AN OPPORTUNIST

MAJ Phillip L. Roberts, MC, USA; MAJ James H. Knepshield, MC, USA; and LTC Ralph F. Wells, MC, USA, El Paso, Tex,

Arch Intern Med 121(6):568-570, June 1968.

The fungus *Coccidioides immitis* ultimately infects most lifelong residents of highly endemic regions. Progressive primary infection occurs in probably less than 0.2 percent of infected individuals, is more frequent among persons with dark skin, and often is associated with a rising complement fixation titer and loss of prior sensitivity to intradermal coccidioidin. Considering the large number of people infected with this fungus, reports of disseminated coccidioidomycosis associated with corticosteroid therapy are infrequent. In contrast to other fungi, including *Candida, Aspergillus, Mucor,* and *Cryptococcus, Coccidioides* is not generally considered an opportunistic organism. This report concerns a patient with disseminated coccidioidomycosis complicating primary biliary cirrhosis. The opportunistic potential of *C immitis* is discussed with consideration of the pertinent literature.

Patient Summary

A 56-year-old white woman was admitted to William Beaumont General Hospital Aug 30, 1965, for management of severe hepatic cirrhosis. She was well until 17 years of age when jaundice developed and persisted for about three months. At the age of 42 years, jaundice recurred. Subsequently, pruritus developed, and xanthomas appeared over the palms, antecubital fossae, and periorbital areas. At 52 years of age she was hospitalized because of persistent jaundice and pruritus. Evaluation included exploratory abdominal surgery with open liver biopsy and a normal operative cholangiogram. A diagnosis of xanthomatous biliary cirrhosis was established. Marked improvement in pruritus and considerable resolution of xanthomas followed the administration of cholestyramine resin given orally in a dose of 12 gm daily. In October 1964, at the age of 55, she had acute cholecystitis; radiographic opacifications consistent with cholelithiasis were present. There was progressive deterioration with increasing jaundice, edema, weight loss, and steatorrhea. She was hospitalized for the last time Aug 30, 1965. No history of previous pulmonary disease could be obtained. For the preceding eight years, she lived in an area endemic for coccidioidomycosis; a 1:100 dilution coccidioidin skin test had been negative in September 1964. Physical examination revealed a cachectic and slightly lethargic woman who was deeply jaundiced and had several periorbital xanthomas. There was moderate hepatosplenomegaly and peripheral edema. The remainder of the physical examination was unremarkable. Laboratory studies disclosed the following values: hematocrit, 38 percent; white blood cell count (WBC), 6,400/cu mm, with a normal differential count; and erythrocyte sedimentation rate (Wintrobe), 38 mm/hr. Serum protein was 5.8 gm/100 ml; albumin, 2.5 gm/100 ml. Liver function studies included bilirubin, 21.6 mg/100 ml, with 12 mg/100 ml direct reacting;

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From the Department of Medicine, William Beaumont General Hospital, El Paso, Tex. Doctor Roberts is now at Kirk Army Hospital, Aberdeen Proving Ground, Md; Dr. Knepshield is now at the University of Louisville Medical School, Louisville; and Dr. Wells is currently in Saigon, South Vietnam.

Reprint requests to Kirk Army Hospital, Aberdeen Proving Ground, Md. 21005 (Dr. Roberts).

alkaline phosphatase, 13.4 sigma units; serum glutamic oxalacetic transaminase, 182 units; and serum cholesterol, 377 mg/100 ml. Serum calcium was 8.7 mg/100 ml. Stools were positive for fat with Sudan stain. Chest x-ray film was normal.

Shortly after admission the patient became stuporous; slight improvement occurred following protein restriction and neomycin administered orally. On Oct 6, she complained of left pleuritic pain. Moist rales were heard in the left lung base, and chest x-ray film showed discoid atelectasis in this area. There was no fever. Chloramphenicol, 2 gm daily, was given for five days starting Oct 5; she received nitrofurantoin, 400 mg daily, for the remainder of the hospital course because of a resistant urinary tract infection. On Oct 25, prednisone therapy was started in a dose of 40 mg daily and continued for ten days but did not improve her condition. She deteriorated rapidly and became comatose Nov 17. Cyanosis and marked respiratory distress were present. Crepitant rales were heard throughout both lung fields. Rectal temperature was 97.8 F (36.6 C). The WBC was 24,400/cu mm, with a shift to the left. There was no eosinophilia. The patient died Nov 17, 1965.

Autopsy revealed severe biliary cirrhosis and cholelithiasis. There was diffuse necrotizing pneumonia bilaterally. The spleen contained numerous microabscesses. Sporangia of *C immitis* were identified in the lungs, spleen, and bone marrow.

Comment

The patient had disseminated coccidioidomycosis complicating severe hepatic cirrhosis; the role of corticosteroids is conjectural. These agents, however, have been shown to enhance certain experimental fungal infections. Newcomer et al, in a well controlled study, concluded that cortisone had an adverse effect on the longevity of mice infected with *C immitis*. This effect was minimal and did not appear to parallel increasing dosages of the drug. Cortisone produced earlier maturation and multiplication of the organism. Redaelli et al injected *C immitis* subcutaneously into both cortisone treated and untreated rats. Three of five treated animals showed diffuse infection of the spleen and lungs, while the control group had only local tubercle-like granulomas. These investigators felt that the production of connective tissue was inhibited in the cortisone treated animals. Much of the experimental work has involved massive fungal challenge or inordinately high dosages of corticosteroids, making extrapolation to clinical situations difficult.

Corticosteroids have been advocated as adjunctive therapy in coccidioidomycosis. Levan and Einstein reported 19 patients with coccidioidal erythema nodosum and erythema multiforme treated with cortisone, 350 to 775 mg over four to six days. All patients were afebrile within 48 hours, and there was rapid improvement in skin and joint manifestations. None developed progressive coccidioidal infection and cutaneous sensitivity to coccidioidin was not impaired. However, the incidence of dissemination in untreated primary coccidioidomycosis is less than one in 500 infected persons, and patients with these allergic phenomena are at an even lower risk.

Since the advent of amphotericin B, the use of corticosteroids has been extended to severe primary and disseminated coccidioidomycosis concomitant with amphotericin B. Such therapy has been designed to ameliorate toxic manifestations of both the coccidioidal infection and amphotericin B. Castellot et al described a 37-year-old woman with myelofibrosis who received 40 mg of prednisone daily. Miliary lung disease became apparent after a 4½-month period of recurrent fever of unknown origin. She did not appear acutely ill until immediately prior to death. Autopsy revealed widespread coccidioidomycosis. DeNardo et al reported a woman with Hodgkin's disease who had received intensive treatment with alkylating agents, irradiation, and antibiotics. Prednisone therapy was started in a dose of 40 mg daily seven weeks prior to death and subsequently increased to 100 mg/day. Autopsy disclosed residual Hodgkin's disease and disseminated coccidioidomycosis. Hileman presented a 59-year-old woman with advanced rheumatoid arthritis treated with corticosteroids and corticotropin. She died with fulminating coccidioidomycosis. *Coccidioides immitis* was recovered from three ante mortem blood cultures.

Lipschultz and Liston reported two patients with disseminated coccidioidomycosis following prednisone therapy. A 41-year-old man had chronic lymphocytic leukemia and was given 40 mg of prednisone daily for ten weeks prior to death; *C immitis* was cultured from ante mortem blood. A 30-year-old man with sarcoidosis was treated with prednisone. Four months later he was found to have a primary coccidioidal infection and steroids were discontinued. Subsequently, there was evidence of dissemination to the right femur for which he was successfully treated with amphotericin B.

At the Second Coccidioidomycosis Symposium, four patients were described who developed dis-

seminated coccidioidal infections following corticosteroid therapy. An 84-year-old woman with idiopathic thrombocytopenic purpura, a 71-year-old man with chronic lymphocytic leukemia, and a 53-year-old woman with Laennec's cirrhosis died with disseminated coccidioidomycosis following corticosteroid therapy. A 28-year-old man was treated with prednisone for chronic stomatitis. Subsequent biopsies disclosed lymphosarcoma. Corticosteroids were continued, in addition to irradiation and mercaptopurine. *Aspergillus* and *Coccidioides* were grown from both sputum and blood cultures with further confirmation at necropsy. The areas of coccidioidal involvement were said to be strikingly free of marginal cellular reaction.

Jones and Spivey described another patient with dual infection by *Coccidioides* and *Aspergillus* associated with corticosteroids. A 53-year-old man had "drug-induced" systemic lupus erythematosus while being treated with isoniazid, pyridoxine hydrochloride, and aminosalicylic acid for presumed pulmonary tuberculosis. First strength purified protein derivative and 1:100 coccidioidin skin tests were positive; cultures for tubercle bacilli and fungi were negative. He was treated with prednisone in a dose of 80 mg daily which was discontinued after 2½ months. Progression of the pulmonary disease with cavitation was coincident with steroid therapy; sputum cultures became positive for *C immitis* and *Aspergillus*. Treatment with amphotericin B was followed by roentgenographic improvement and the appearance of an intracavitary mycetoma.

Cytotoxic and immunosuppressive agents may have caused some of these patients to be more vulnerable to progressive coccidioidal infection. Winn described a patient with coccidioidal meningitis who was treated with amphotericin B. Nephrotoxicity of amphotericin B necessitated renal transplantation. Approximately six weeks after initiating immunosuppression with azathioprine and cactinomycin, the patient had a clinical and serologic relapse of meningitis.

Corticosteroids can enhance experimental coccidioidal infections. The role played by these hormones in the clinical situation is less certain, since in most instances the patients were chronically debilitated or had an underlying disease known to impair immunologic response. Also, disseminated coccidioidomycosis has been observed to complicate similar disease states in the absence of corticosteroids. Available evidence, however, suggests that *C immitis* does have significant opportunistic potential in that infection can be enhanced under certain adverse host circumstances. This is supported by experimental work and increasing clinical reports which include two patients with co-existing coccidioidal and aspergillus infections in the presence of abnormal immune responsiveness and corticosteroid therapy. Although corticosteroids can be valuable adjunctive therapy with concomitant chemotherapy, their use should be tempered with appreciation of this opportunistic potential, especially in patients with debilitating diseases and altered immune response.

Summary

A patient with disseminated coccidioidomycosis complicating severe biliary cirrhosis is reported. Corticosteroids were given during ther terminal illness. Further cases are cited from literature and evidence presented which suggests that *Coccidioides immitis* has significant opportunistic potential.

Generic and Trade Names of Drugs

Cholestyramine resin—*Cuemid, Questran.*

Chloramphenicol — *Chloromycetin, Cylphenicol, Tega-Cetin.*

Nitrofurantoin—*Furadantin.*

Prednisone—*Deltasone, Deltra, Meticorten, Paracort, Cotone.*

Cortisone acetate—*Cortogen Acetate, Cortone Acetate.*

Amphotericin B—*Fungizone.*

Corticotropin—*Acthar, Actrope, Duracton.*

Mercaptopurine—*Purinethol.*

Isoniazid—*Armazide, Cotinazin, Niconyl, Nidaton, Nydrazid.*

Pyridoxine hydrochloride—*Beadox.*

Aminosalicylic acid—*Pamisyl, Para-Pas, Parasal, Propasa, Rezipas.*

(The omitted figure and references may be seen in the original article.)

PATHOLOGY OF THE LUNG IN FATALLY BURNED PATIENTS

CAPT F. Daniel Foley, MC, COL John A. Moncrief, MC, Arthur D. Mason, Jr., MD, From US Army Surgical Research Unit, Brooke Army Medical Center, Fort Sam Houston, Texas 78234, Ann Surg 167(2):251-264, February 1968.

While direct thermal damage to the lower respiratory tract has been demonstrated to occur only with the inhalation of steam, respiratory complications are a common fatal factor in patients sustaining thermal injury. Some clinical studies implicate inhalation of irritating products of combustion as the primary cause of respiratory complications and recent reports of a high rate of pulmonary lesions associated with facial burns have been interpreted as reinforcing this premise. Our experience, however, indicates that tracheobronchitis and pneumonia often are not directly related to facial burns or inhalation injury and are frequently a complication of tracheostomy, a procedure common in the immediate postburn period. The difficulty in separating respiratory complications due to inhalation injury from those due to tracheostomy is further compounded by the problem of clinically differentiating respiratory distress due to intrinsic pulmonary complications, from that due to alterations in cardiovascular hemodynamics following extensive burns, or as a compensatory response to acid-base imbalance. Evaluation is especially difficult when the study group also contains elderly patients who may have unrecognized as well as overt pre-existent cardiorespiratory problems.

The study reported herein attempts to clarify some of these difficulties by defining pathologic aspects of pulmonary complications that occur following cutaneous burns. The study group is unique in that it consists largely of active duty military personnel and their dependents, who are virtually free of significant pre-existent repiratory disease. The necropsies represent the largest group so studied and were performed by pathologists who autopsied burned patients almost exclusively and therefore were aware of the peculiarities of such autopsies. The pathologists at this installation customarily make daily rounds with the surgeons and the opportunity of following the clinical course of each patient renders the interpretation of the autopsy findings singularly appropriate.

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Material

There were 243 deaths from burns and 233 autopsies performed at the US Army Surgical Research Unit from 1960 through 1965 (autopsy rate, 96 percent). During the same period, a total of 817 patients were hospitalized for treatment of burns and Table 1 lists the types of burns encountered in both groups. Ninety percent of patients at autopsy had sustained flash or flame injuries. Patients who sustained electrical injury without flame burns were excluded from the study group.

Distribution of autopsied patients by age and extent of thermal injury demonstrates the relative youth and magnitude of burns in patients received at this unit (Tables 2, 3). Over 90 percent of burned patients treated during this period were under 50 years of age and this is accurately reflected in the autopsy population since over 90 percent of patients dying with burns were below 50 years of age. Also, 50 percent of patients treated had sustained over 30 percent total body area burns and patients with burns of this magnitude accounted for 95 percent of deaths and autopsies.

All autopsy protocols, clinical summaries and tissue sections from the respiratory system were reviewed. A total of 1,821 histological sections of the respiratory tract, an average of 7.8 per autopsy, were available to study. Paraffin blocks were recut and restained and additional special stains were done when necessary. The pathologic diagnoses in the respiratory system were listed after review of the clinical and gross autopsy data and personal review of all sections. In addition, the causes of death were reviewed and determined from the clinical and pathologic material.

Results

Cause of Death. The major cause of death during the period 1960-3 was burn wound sepsis which, as previously defined, is due to massive bacterial invasion of the burn wound. In 1964-5, topical chemotherapy of the burn wound with Sulfamylon was instituted which significantly reduced mortality from burn wound sepsis and the major fatal complication

TABLE 1. *Type of Burns Encountered in Patients Treated and in Autopsy Population*

Year	No. Patients*		Flash and/ or Flame	Electrical	Steam	Hot Liquid	Chemical	Contact
	Hospitalized	Autopsied						
1960	96	30	78 (23)	2 (2)		11 (5)	1	4
1961	88	30	76 (29)			8 (1)		4
1962	142	51	124 (46)	2		13 (5)	3	
1963	148	56	136 (54)	1	1 (1)	9 (1)		1
1964	184	34	147 (31)	7 (1)	2 (1)	24 (1)	3	1
1965	159	32	125 (28)	6 (1)	1	17 (2)	4 (1)	6
TOTAL	817	233	686 (211)	18 (4)	4 (2)	82 (15)	11 (1)	16 (0)

* No. in ( ) represents autopsies.

TABLE 2. *Distribution of Patients by Age and Percent Mortality*

Age	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	Total
No. burned	228	101	232	138	62	29	17	7	3	817
Deaths	79	27	46	42	29	11	3	4	2	243
% Mortality	35	27	20	30	47	38	18	57	67	29.7
Autopsies	78	27	44	38	28	10	3	4	1	233

shifted to the respiratory system. The decline in burn wound sepsis as a cause of death in reference to both admissions and total deaths during 1964-5, compared to 1960-3, is highly significant ($p < 0.001$). The successful control of bacterial invasion of the burn wound with Sulfamylon has been reported.

The major cause of death revealed at autopsy in all 233 burned patients is given in Table 4. Death was attributed to septicemia when one or more antemortem blood cultures were positive for bacteria in association with clinical features of sepsis and a source of infection that was determined at autopsy. In the absence of a source of infection elsewhere, septicemia was considered to be of pulmonary origin when extensive pneumonia was present clinically and confirmed at autopsy. Deaths with septicemia associated with pneumonia showed a proportionate increase in 1964-5 compared with 1960-3 due to decline in sepsis originating from invasive infection of the burn wound. A third and increasingly frequent cause for septicemia in the burned patient is suppurative phlebitis that involves cannulized veins (Table 4). Deaths attributed to sepsis also occurred in one patient with suppurative cholecystitis and in one patient with a mandibular abscess, and this accounts for the two patients listed in Table 4 with miscellaneous sources of infection. Patients who had positive blood cultures and were considered to have septicemia clinically, and in whom necropsies did not disclose an origin of infection, were categorized as having septicemia of uncertain origin.

The mortality table (Table 4) underestimates the true incidence of suppurative phlebitis as well as Curling's ulcers in burned patients since these complications are successfully treated in most instances. Seven of 8 patients whose cause of death was gastroduodenal ulceration died from repeated episodes of hemorrhage; one died from peritonitis following perforation of a duodenal ulcer.

Those deaths attributed to renal failure have been due to inadequate resuscitation in the early postburn period and no deaths were placed in this category when renal insufficiency was but a terminal feature of the major cause of death, for example, burn wound sepsis. There were eight deaths attributed to renal failure on the basis of oliguria with a rapidly rising serum potassium. In addition, there were five deaths attributed to severe hypotension in the early postburn period that are listed in the miscellaneous category and these were also thought to have resulted from inadequate restoration of fluid and colloid. There were, therefore, 13 deaths in these two groups that might be considered as deaths due to inadequate resuscitation prior to evacuation to this unit.

Other causes of death in the miscellaneous group include: coronary heart disease (4), acidosis (3), adrenal hemorrhage (2), pancreatitis (2), pulmonary emboli (2), peritonitis (2), cerebral vascular thrombosis (1), hepatic cirrhosis (1), subacute

TABLE 3. *Distribution of Patients by Extent of Total Body Burn and Percent Mortality*

% Body Burn	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90+	Total
No. burned	150	146	126	103	80	71	46	49	46	817
Deaths	1	5	7	26	40	39	37	43	45	243
% Mortality	0.7	3	6	25	50	55	80	88	98	29.7
Autopsies	1	5	7	23	40	39	35	39	44	233

TABLE 4. *Cause of Death in 233 Fatally Burned Patients*

	1960	1961	1962	1963	1964	1965
Septicemia, origin, burn wound infection	18	15	31	34	3	4
Septicemia, origin, respiratory infection	(3)	(5)	(3)*	(1)*	(2)	(6)
Septicemia, origin, phlebitis		1		2	1	2
Septicemia, origin, miscellaneous		1	1			
Septicemia, origin, uncertain	2	3	4	2		1
Respiratory disease	5	5	3	6	12	13
Gastrointestinal ulceration			3	2	2	1
Renal failure			2	2	2	2
Miscellaneous	1	1	2	8	9	4
Cause of death uncertain	4	4	9	7	7	11
Deaths	30	31	54	57	37	34
Autopsies	30	30	51	56	34	32
Patients treated	96	88	142	148	184	159
% Mortality	31.3	35.2	38.0	38.5	20.2	21.4

( ) Subtotal, already listed under Respiratory Disease.
*Also had other possible causes for sepsis.
Note: There are more causes of death listed than patients who were autopsied since two causes of death were occasionally considered of equal importance.

bacterial endocarditis (1), aortic-esophageal fistula (1), and retroperitoneal hemorrhage (1).

In the category, "Cause of Death Uncertain" are many patients who died, often within the first week postburn, with pulmonary edema and congestion as the sole finding at autopsy, in addition to the burn. There are also a few patients in this group whose death was a puzzle to the clinician and pathologist although there may have been no lack of autopsy findings.

Pneumonia. Table 5 lists the pathologic findings in the lungs of the 233 patients at autopsy and indicates those considered a cause of death. We have used the term "airborne pneumonia" in preference to bronchopneumonia or lobar pneumonia so as not to confuse this complication with the pneumonic lesions that we believe to be hematogenous in origin. This distinction is important because no deaths were attributed to hematogenous pneumonia, but rather to the original infective complication that resulted in dissemination to the lung, e.g., burn wound sepsis or suppurative phlebitis. In contrast, airborne pneumonia, which was found in 69 burned patients at autopsy, was considered a major cause of death in 37 patients. This type of pneumonia was listed as a cause of death, in addition to the burn, when progressive lower respiratory infection was dominant in the clinical course and extensive inflammatory consolidation of pulmonary parenchyma was found at autopsy. Although noted annually as the leading cause of respiratory deaths, airborne pneumonia has increased in frequency and has replaced burn wound sepsis as the major cause of death in 1964-5. The increased incidence of pneumonia is of more significance in reference to deaths ($p<0.01$) than total admissions ($0.05<p<0.1$) when both periods are compared. Pneumonia has recently been more of a problem in our adult population and this is substantiated if one compares the incidence of fatal pneumonia in hospitalized patients over 15 years of age during each period. Twelve of 318 adult patients died of pneumonia during 1960-3 vs. 19 of 237 patients during 1964-5 ($p<0.05$).

The pathologic aspects of airborne lower respiratory infection were demonstrated by the usual suppurative response in a bronchopneumonic, lobular or

TABLE 5. *All Fatal and Non-Fatal Pulmonary Complications in 233 Burn Autopsies*

	1960		1961		1962		1963		1964		1965	
	Total	COD*	Total	COD	Total	COD	Total	COD	Total	COD	Total	COD
Pneumonia, airborne with hyaline membranes	7	4 (1)	8	4 (1)	11	2 (0)	13	6 (2)	15	9 (7)	15	12 (7)
Pneumonia, hematogenous	5		11		25		11		1		1	
Tracheobronchitis, erosive	17	1	20	1	18	1	24		13	2	17	1
Laryngeal ulceration	8		4		5		7		1		2	
Pulmonary thromboemboli with infarction	13 (6)	1	9 (2)		8 (2)		16 (1)		5 (3)	1	8 (1)	
Pneumothorax tracheostomy complication	2 (1)		3 (3)		2 (2)		2 (1)		2 (2)	1	2 (1)	
Preexistent pulmonary disease	2		3				2		6	1	3	1
Miscellaneous:												
Pulmonary edema and congestion	15		20		32		42		26		22	
Atelectasis					5		1		2			
Pulmonary megakaryocytes	3		9		11		13		2		11	

* COD—Cause of Death ( )—Subtotal

TABLE 6. *Bacteria Cultured From Sputum, Tracheal Secretions and Postmortem Lung Cultures in 37 Burned Patients Dying from Bronchopneumonia*

	1960–1963		1964–1965	
	Ante-mortem	Post-mortem	Ante-mortem	Post-mortem
Aerobacter—E. coli	5	6	10	17
Pseudomonas sp.	6	3	6	12
Staphylococcus aureus	4	6	2	5
Proteus sp.	1	3	3	9
Miscellaneous	5	6	3	11
TOTAL	21	24	24	54

lobar distribution with varying degrees of organization, in a few cases, that were consistent with the duration of this complication. Table 6 lists all the organisms cultured from sputum or tracheal secretions and postmortem lung cultures in the 37 patients dying of pneumonia. Mixed gram-negative infections were commonly encountered throughout the entire period. Both antemortem and postmortem cultures frequently yielded coliform organisms particularly during 1964-5. It was not uncommon however to recover coagulase-positive *Staphylococci* from initial sputum cultures which subsequently yielded gram-negative organisms following potent antistaphylococcal chemotherapy.

Certain unique pathologic features became prominent in the lungs of patients dying from airborne pneumonia in 1964-5. Pulmonary hyaline membranes have previously been noted in fatally burned patients. Hyaline membranes were found in 4 of 16 patients who died from pneumonia in 1960-3. In the 1964-5 group of 21 patients whose cause of death was pneumonia, 14 had hyaline membrane formation ($p<0.05$). There were additional histologic features in the areas of pneumonia and hyaline membrane formation that were not thought to represent the customary pulmonary response to bacterial infection alone. These included hypervascularity and thickening of the alveolocapillary membrane due to interstitial edema and inflammation. Also, there were numerous alveolar macrophages and septal epithelial cells lining the alveoli.

The pulmonary lesion secondary to hematogenous dissemination was common during 1960-3 when burn wound sepsis was prevalent, but was not considered an intrinsic respiratory complication. This lesion is believed to evolve from dissemination of bacteria from the infected burn wound to the lung. The pathologic features of hematogenous pneumonia are described in the discussion. This and other embolic visceral lesions originating from infection of the burn

wound have been noted previously. Postmortem bacteriological cultures of lungs with hematogenous pneumonia yielded *Pseudomonas sp.* and *Staphylococcus aureus* as the most frequent pathogens, but other gram-negative organisms were frequently present.

Tracheobronchitis. The most frequent intrinsic pulmonary complication following thermal injury is tracheobronchitis, which was manifest at autopsy in 109 patients—almost half of all autopsies. During the 6-year period, erosive tracheobronchitis due to abutment of the tracheostomy tube on the anterior tracheal wall has been a direct cause of death in 6 patients (Table 5). In two, the erosion was deeply invaded with bacteria, with peritracheitis and positive antemortem blood cultures, in the absence of infection elsewhere in the lung or burn wound. Another patient developed mediastinitis via bacterial invasion of the eroded trachea. Diffuse invasive bacterial tracheobronchitis occurred in one patient and was thought to have originated in the tracheal ulcer. Two patients died with hemorrhage from the anterior tracheal erosion. The lesions encountered in the tracheobronchial tree and their relation to tracheostomy and suspected inhalational injury are presented in the discussion.

Tracheostomy may have been indirectly responsible for other deaths although not listed as such in Table 5, *e.g.,* patients who die of pneumonia subsequent to temporary obstruction of a main stem bronchus by the tracheostomy tube early in the course of treatment. Also, in patients who develop pneumothorax as a tracheostomy complication, death may be attributed to the pneumothorax, as in one of our patients, or to the subsequent development of pneumonia. In addition, bacterial infection of tracheal erosions may represent a nidus for airborne dissemination of lower respiratory infection. In any case, the hazards of tracheostomy in the burned patient are underestimated by the mortality table.

Laryngitis. Laryngeal ulcerations were found in 27 autopsies. This is an underestimate of incidence since the larynx was not described in adequate detail in some autopsies. Of the 27 examples that were available for study, 21 involved the vocal or ventricular folds. The remainder of the erosive lesions occurred just above or below the folds or over the corniculate process or epiglottis. Bacterial infection of these lesions was demonstrated in 20 of the 27 autopsies.

Thromboemboli. Thrombi, without bacteria, were found in the lungs of 59 burned patients at autopsy and were assumed to be embolic in nature. These were usually of microscopic proportions, involved pulmonary arterioles and small musculo-elastic pulmonary arteries 100-200 micra in diameter and were few in number in relation to the total cross-sectional area of the pulmonary vasculature. Pulmonary infarcts were occasionally encountered, as indicated in Table 5, and these were associated with thromboemboli that were observed grossly. In 1960, a 7-year-old boy died following hemoptysis of an estimated 950 ml., eight days after sustaining 35 percent total body burns. A large right lower lobe pulmonary infarct and pulmonary thromboemboli, both recent and organizing, were found at autopsy. In 1964, a 26-year-old man died 14 days after sustaining 65 percent total body burns. Pulmonary infarcts were found at autopsy with recent thromboemboli in each main pulmonary artery. These two fatal complications were not classified in the mortality table as deaths due to respiratory disease.

Pneumothorax. Thirteen patients had pneumothorax sometime during their course. However this is another complication that is underestimated in a study limited to fatally burned patients. The pathogenesis of pneumothorax in burned patients almost invariably evolves from tracheostomy complications rather than from trauma to the chest at the time of thermal injury. The single patient who died *directly* after pneumothorax was a 30-month-old infant who sustained 80 percent total body burns 2 days previously. Tracheostomy had been placed between the 7th and 8th tracheal rings prior to evacuation to this unit and he subsequently developed mediastinal emphysema and bilateral pneumothorax.

Chronic Pulmonary Disease. Pre-existent pulmonary disease has been a significant factor in mortality in only two patients over the 6-year period. One was a 61-year-old man who had previously undergone pneumonectomy for bronchogenic carcinoma and at autopsy his opposite lung was emphysematous with acute tracheobronchitis. The second was a 75-year-old man who had acute bronchopneumonia superimposed on severe chronic bronchitis and emphysema.

Miscellaneous. Pulmonary edema and congestion is the most frequent autopsy finding in the lungs of burned patients, but is considered an unrevealing pathologic diagnosis. Although it is frequently the only finding in patients with extensive burns who die in the early postburn period, no effort was made to correlate this finding with examples of overhydration, renal failure, cardiac arrest with and without arrhythmias, or other clinical events that might result in

pulmonary edema and congestion since retrospective clinical material is incomplete and arbitrary in this regard, and also because pulmonary edema and congestion may develop rapidly as an agonal phenomenon. Atelectasis is another autopsy diagnosis of uncertain significance, but in no instance was it thought to be an important or contributory cause of death.

Pulmonary megakaryocytes were frequently found in increased numbers in burned patients' lungs. This probably reflects a general posttraumatic response in which megakaryocytic production or mobilization from bone marrow is increased and entrapment in the pulmonary capillaries occurs.

Other features could not be evaluated or were thought not to be of any unique interest, e.g., pulmonary septal macrophages are prominent in most lungs of burned patients, however, this response is probably too nonspecific to warrant meaningful interpretation. The frequency of pulmonary fat emboli could not be properly evaluated since the tissue available was paraffin-embedded and therefore had been processed through fat solvents. Insignificant foci of bronchiolitis, pleuritis overlying areas of pneumonia and small inactive pulmonary granulomas were considered irrelevant. Pleural effusion and small foci of intra-alveolar hemorrhage were invariably associated with pulmonary edema and congestion and were not individually analyzed.

Discussion

There is no readily apparent reason for the recent increase in deaths due to pneumonia in our adult population. Although the incidence of burn wound sepsis declined in the period 1964-1965, the increase in pneumonia as a cause of death does not appear simply for lack of a better cause since the clinical and pathologic interpretation of death *from* pneumonia was consistent during both periods. Also many patients died *with* small foci of pneumonia that were considered insignificant in 1964-5 as they were in 1960-3. The average extent of total body burn has also remained fairly constant throughout the entire 6-year period. Furthermore, fatally burned patients are not surviving longer in the absence of burn wound sepsis to subsequently develop pneumonia since the distribution of patients as to the postburn day on which death occurred reveals no difference between patients who died of burn wound sepsis and those who died of pneumonia, during either period. Although tracheobronchitis in our patients has been associated with tracheostomy, as discussed below, the increase in fatal pneumonia is not similarly related. Tracheostomy was performed in 30 percent of 474 burned patients treated from 1960-3 and in 21 percent of 343 patients treated in 1964-5. The number of tracheostomies performed on fatally burned patients during the above periods was 56 percent (96 of 172) and 61 percent (43 of 71), respectively. Also, there has been no increase in inhalational injury, either suspected clinically or documented at autopsy, that might account for the rise in deaths due to pneumonia.

Hyaline membrane formation and hyperplasia of alveolar lining cells with congestion and interstitial edema of the alveolocapillary membrane represents a constellation of unique histologic features that we have seen previously in the lungs of burned and nonburned patients who received prolonged positive pressure ventilatory assistance with oxygen. Since these pathologic findings were significantly more frequent in lungs of patients dying from pneumonia during 1964-5 (Table 5) and were concurrent with an overall increase in deaths due to pneumonia during this period as compared with the 1960-3 period, we examined the utilization of ventilatory assistance and oxygen in patients who died from pneumonia both with and without these unique pathologic features. Thirty-four records of 37 patients dying from pneumonia were available to study. Eleven of 17 patients with, and 10 of 17 patients without hyaline membrane formation and the associated histologic alterations described above, received positive pressure ventilatory assistance with an oxygen source. Hyaline membranes have also been seen in association with oxygen therapy, however, all patients dying from pneumonia in our group, both with and without hyaline membranes, received oxygen at some time in their terminal illnesses. There was no difference therefore in the use of ventilatory assistance or oxygen *per se,* in patients with or without hyaline membrane formation. These histologic findings have been attributed by others to oxygen and positive pressure ventilatory assistance, particularly when this type of inhalational therapy is given for prolonged periods, viz., over 10 days. We are unable to analyze the association of hyaline membrane formation with duration of ventilatory assistance and level of oxygen tensions achieved due to limitations in the retrospective study. Increased incidence of hyaline membrane formation and the associated histologic changes, during 1964-5, may be the result of earlier and more prolonged use of oxygen and positive pressure ventilatory assistance in burned

patients who display respiratory symptoms. There is no question that this histologic response has not only become more frequent, but has increased in extent in the lungs of patients dying from pneumonia in the last two years of the study. Furthermore, this unique histologic response also occurred in areas of gross pulmonary consolidation that were free of suppuration and bacteria and therefore presumably free of bacterial infection. The increased extent of pulmonary consolidation and consequently the increased frequency of deaths attributed to pneumonia during 1964-5, therefore, may be partly a result of respirator or oxygen toxicity.

During 1964-5, due to control of septicemia originating from infection of the burn wound, hematogenous pneumonia virtually disappeared from autopsy subjects, except for isolated examples, some of which originated from an infected cannulized vein. The pathologic features of this type of pneumonia are distinct and readily recognized. The lesions are commonly small, subpleural, hemorrhagic and discrete, or may be confluent. The larger single lesions characteristically resemble pulmonary infarcts. Focal necrosis of alveoli is presently histologically and in hematogenous *Pseudomonas* lesions there are myriads of gram-negative bacteria proliferating in the alveolocapillary membrane and particularly in the perivascular and peribronchial spaces. Although the peribronchiolar sheath may be filled with gram-negative bacteria, the early lesion is relatively free of exudate within the bronchiolar lumen, thus distinguishing it from bronchopneumonia. Staphylococcal emboli, however, did not show this perivascular distribution even though nests of cocci were found within vessels. The hematogenous derivation of this type of pneumonia is also suggested by the frequent presence of fibrin and neutrophil thrombi containing bacteria, in the small pulmonary arteries and arterioles within the lesions.

Although tracheobronchitis is the most frequent finding in the lungs of fatally burned patients, the prominent lesions encountered in the present study were clearly related to tracheostomy in most instances, rather than to inhalation injury. Ninety-nine of the 109 patients with tracheobronchitis had tracheostomies performed. The lesions that are convincingly tracheostomy complications include erosions or ulcers due to abutment of various parts of the tracheostomy tube or its inflatable cuff on the tracheal mucosa. Erosions in the tracheobronchial mucosa beyond the range of the tracheostomy tube occurred less frequently, but were also focal and thought to be traumatic due to frequent suctioning. These erosions may become infected, as noted previously, with the development of bacterial tracheobronchitis.

Although similar lesions were occasionally found at the margin of the vocal folds, laryngeal and tracheal mucosa above the tracheostomy stoma was grossly normal in the majority of patients at autopsy who had tracheitis. The normality of the laryngeal mucosa, when focal erosions were present below the tracheostomy stoma, is regarded as further evidence that tracheobronchitis is not due solely to inhalation injury, the effect of which might be expected to be diffuse or at least manifest proximal as well as distal to the tracheostomy stoma. Nevertheless, clinical evidence for thermal or chemical laryngotracheitis due to inhalation injury exists. We frequently see severely burned patients with marked dyspnea and bronchospasm postinjury and with carbonaceous sputum, whose laryngeal and tracheal mucosa is inflamed and edematous at bronchoscopy, prior to the performance of a tracheostomy. A tracheostomy is invariably performed, however, and if the injury is fatal, the lesions commonly seen at autopsy are those related to the tracheostomy.

The interpretation of the discrepancy between clinical evidence for inhalational injury and the lack of autopsy documentation, is twofold. Carbon deposition and thermal necrosis of laryngeal and upper tracheal epithelium is frequent in patients who die in fires and this evidence of inhalational injury is commonly recorded by forensic pathologists. The experience of pathologists who autopsy patients who survive cutaneous thermal injury beyond the burn day, however, is in contrast to pathologists who examine those who died in fires. We have demonstrated soot deposit and thermal necrosis of laryngotracheal mucosa in a few burned patients who expired before the first or second postburn day, but these features are usually absent by the time postmortem examinations are performed. Clinically, we also noted diminishing expectoration of soot beyond the second postburn day and therefore the lack of pathological documentation of inhalational injury is not unexpected since 94 percent of the autopsies were performed beyond the second postburn day. Secondly, the residual of inhalation injury that is encountered above the tracheostomy site has been minimal in comparison with the extensive, ulcerative tracheitis due to the tracheostomy tube in the lower trachea. Since the carbon deposit and necrotic respiratory epithelium has been expectorated, the residual inflammatory infiltrate in the lamina propria of the respiratory mucosa, with regeneration of respira-

tory epithelium, above the level of the tracheostomy, is overshadowed by the impressive gross and histologic alterations inferior to the tracheostomy.

We think that a combination of factors is responsible for the focal ulcerative laryngeal and tracheal lesions found in fatally burned patients. The lesions mechanically related to trauma from the tracheostomy tube seem to occur more readily following suspected inhalation injury. Similar erosions limited to the vocal folds with a normal surrounding laryngeal mucosa may also represent the combined effects of laryngitis due to inhalation injury in combination with the trauma of endotracheal intubation, e.g., during anesthesia, or simply from voice trauma. Our findings are consistent with Moritz's experimental studies on the occurrence and location of inhalational thermal injury and also suggest that inhalational laryngeal or tracheal injury undergoes rapid repair in the absence of superimposed trauma. The focal ulcerative lesions that occur so frequently in the tracheobronchial tree emphasize the hazards of tracheostomy in the burned patient.

The association of facial burns with respiratory complications implies that inhalation injury may occur at the time of burning and result in tracheobronchitis and pneumonia. For purposes of discussion patients with facial burns include those with over 1 percent of total body surface, partial or full thickness, burn that involves the anterior face between the eyes and chin and between each malar eminence, i.e., around the nose or mouth. Thirty-eight of 498 patients with facial burns and 5 of 319 patients without facial burns died from tracheobronchitis or pneumonia ($p<0.01$). Although these data support the premise that fatal respiratory complications occur more frequently with facial burns, we think it is equally important that the majority of fatally burned patients with facial burns died from nonrespiratory complications over the 6-year period. Of 187 patients, at autopsy, who had facial burns, 149 died of complications other than tracheobronchitis or pneumonia (80 percent).

If thermal injury around the nose or mouth implies that inhalation injury is responsible for subsequent respiratory complications, then one might expect to encounter respiratory complications in patients who suffer facial burns without extensive thermal injury elsewhere. There were 59 patients treated over this 6-year period who sustained facial burns, as defined above, in association with less than 15 percent total body surface thermal injury. Not one suffered either a fatal or nonfatal respiratory complication. This supports the premise that facial burns alone do not constitute a hazard to the burned patient. Also, there was no difference in mortality between the 498 patients with, and 319 patients without facial burns, using probit analysis ($LD_{50} \cong 50$ percent total body surface burn).

All deaths attributed to tracheobronchitis or pneumonia, in association with facial burns, occurred in patients with over 39 percent total body burns. There were 299 patients with 39 percent, or more, total body surface burns and 241 had facial burns (81 percent). The increased frequency of respiratory complications in patients with facial burns, therefore, may indicate that severely burned patients are more prone to develop tracheobronchitis and pneumonia for reasons other than inhalation injury since extensive thermal injury occurs more often with, than without, facial involvement.

Summary and Conclusions

A clinicopathological examination of 233 autopsies was performed to analyze the frequency of fatal complications following cutaneous thermal injury with particular reference to pulmonary complications.

Over a 6-year period, the major fatal complication in burned patients treated at the Surgical Research Unit has shifted from invasive burn wound infection to pneumonia. The decline in burn wound infection has been due to effective topical chemotherapy. The recent increase in deaths attributed to pneumonia is considered real in patients over 15 years of age and results from the greater frequency of infective lower respiratory disease found clinically. A part of the increase in deaths attributed to pneumonia may be due to effects of earlier and more prolonged ventilatory assistance and oxygen therapy.

Although inhalational injury occurs, our experience indicates that the majority of laryngeal and tracheal lesions found at autopsy are due to repeated trauma from tracheostomies or endotracheal tubes.

Respiratory complications occur more frequently in patients with facial burns, but the presence of facial burns alone does not constitute a particular hazard to the burned patient. The increased incidence of respiratory complications in patients with facial burns, in our material, may be due to the increased occurrence of facial burns in severely burned patients who are more susceptible to infective lower respiratory disease. Respiratory complications in less severely burned patients with facial burns have not occurred.

(The figures and references may be seen in the original article.)

REACTIONS PECULIAR TO TRANSURETHRAL RESECTION OF THE PROSTATE

C. D. Creevy, MD, Surg Clin N Amer 47(6):1471-1472, December 1967.*

Certain peculiarities in the technique of transurethral prostatic resection can cause reactions not produced by other operations, although they may occur in other situations. Predisposing factors inherent in the operation itself consist of (1) the need for a continuous flow of irrigating fluid to ensure clear vision and (2) electrolysis, by the current which energizes the wire loop, of salts released by the blood from the cut surfaces.

Exciting causes include (1) opening sizeable prostatic veins with low intraluminal pressures; (2) entrance into them of irrigating fluid, particularly by overdistention of the bladder; and (3) ignition of the hydrogen and oxygen released through electolysis.

Hemolysis

Only three kinds of reactions need be considered here. The first of these is hemolysis when distilled water is the irrigating fluid. This may result from the entrance into the circulation either of the distilled water itself, or of water containing blood already hemolyzed in the bladder. If the consequent hemoglobinemia is intense enough, hemoglobinuric nephrosis may lead to renal failure, the severity of which may be greatly aggravated by pre-existing renal lesions or by an episode of hypotension.

Such a reaction is manifested by cyanosis, mental confusion or even stupor, hemoglobinemia and hemoglobinuria (the latter masked by postoperative bleeding), jaundice, and late hypertension. The identity and occurrence of this reaction were proved as follows: The plasma hemoglobin was measured at the beginning and end of transurethral prostatic resection. When distilled water was used for irrigation, there was a fifteen-fold increase. This did not occur from the use of intravenous fluid nor from the use of diathermy during open operations. When 4 percent glucose was used for irrigation, the plasma hemoglobin did not rise.

In addition, the blood sugar was also measured at the beginning and end of resection. With distilled water it remained constant; with 4 percent glucose it rose to two and one-half times the preoperative level. None of the approximately 300 patients in this study was transfused.

In addition, Dr. E. T. Bell studied sections of the kidneys of six patients dying of uremia prior to this study. Two showed the characteristic pigmented casts and tubular lesions of hemoglobinuric nephrosis.

The problem was solved completely by using an isotonic nonelectrolyte for irrigation (an electrolyte diffuses the current from the loop so that it will not cut).

TUR (Resectionist's) Reaction

The second type of untoward response to transurethral resection has been called the "TUR reaction" when it is really the "resectionist's reaction." It results from hypervolemia-hyponatremia from entrance into the circulation of a considerable volume of isotonic irrigating fluid. Its effects are magnified by cardiorenal insufficiency.

It is manifested by hypertension, mental confusion, nausea and vomiting, a falling hematocrit, edema, weight gain, hyponatremia, and hypervolemia; circulatory failure may occur. Its occurrence is most readily identified by finding a low serum sodium.

This problem is also easily prevented by avoiding overdistention of the bladder (it must be emptied frequently) during the operation. Others have sought to prevent it by inducing diuresis with mannitol before and during the operation; I have not tried it. Controlled hypotension also helps by lessening bleeding and improving vision without resorting to high irrigating pressures.

When the reaction occurs, one usually needs only to restrict fluid intake for a while. In the more severe cases, one may give a calculated amount of 3 percent sodium chloride intravenously. Cardiac insufficiency requires digitalization. Diuretics are rarely needed.

Intravesical Explosion

This type of reaction may occur when the operator forgets to evacuate the bladder frequently and completely, so that a considerable quantity of hydrogen and oxygen accumulates in the highest part of the bladder. If this is set off by the arc between tissue and loop while the bladder is slack, the explosion merely startles the operator. If the bladder is tense, it will rupture. The solution is self-evident.

* Professor of Urology and Director of Division, University of Minnesota Medical School; Chief of Urology, University of Minnesota Hospitals, Minneapolis, Minnesota.

All of these reactions are, at the present time, due to carelessness; all are easily avoided.

Observances of the precautions outlined above, coupled with the use of potent antibacterial agents, the transfusion of blood only from a reliable bank, and judicious anesthesia have resulted in a surgical mortality of about 0.5 percent, which is probably as low as one can expect in view of the average age of the patients, which is about 70.

MEDICAL ABSTRACTS

ANESTHESIA FOR COMBAT SURGERY

CDR Paul R. Knox, MC USN, Camp Pendleton Symposium on Combat Surgery, Mar 1968.

The administration of anesthesia to battle casualties is a challenging and often 'exciting' experience. Invariably this type of patient presents with (1) extensive wounds (which are often life-threatening), (2) an unknown blood loss, (3) various stages of dehydration, and (4) a potentially full stomach.

Proper preoperative preparation of this type of patient is of the utmost importance if there is to be a satisfactory outcome. This preparation must include not only the necessary resuscitative measures; but also (1) a complete and thorough physical examination, (with all clothing removed and all wounds inspected), (2) the indicated radiological examinations and accurate as possible interpretation of the X-rays, (3) at the minimum a hematocrit determination, and (4) the typing and crossmatching of enough blood.

Although conduction anesthesia might seem preferable in many ways, it was our experience that over two-thirds of these patients required general anesthesia. The reasons why conduction anesthesia was often not the anesthetic of choice were discussed. However, the use of spinal anesthesia, as well as other forms of regional blocks were mentioned.

The problem of a potentially full stomach became more important when general anesthesia was undertaken. It was axiomatic that a fresh combat casualty required an endotracheal tube if general anesthesia was contemplated. A method of crash induction was described as well as the reasons for a crash induction. Maintenance of general anesthesia was, for the most part, 50:50 nitrous oxide: oxygen in a semi-open system plus halothane or penthrane as needed and/or as tolerated by the patient. The advantages of using halothane or penthrane in a hypovolemic patient were discussed. If muscle relaxation was required, d-tubocurarine was the relaxant most often employed since it can be reversed. Not infrequently a Bird anesthesia assistor-controller was utilized not only to insure adequate ventilation but also to give the anesthetist another hand to pump blood, etc.

In order to meet the demands to carefully evaluate the circulatory status of the extensively and/or critically wounded patients; central venous pressure, urinary output, electrocardiogram, temperature, as well as blood pressure and pulse were monitored.

Intraoperative fluid replacement was usually Ringer's lactate but a modification of the schedule recommended by Shires and Jenkins was used. All blood given in the operating room was warmed and 44 meq of sodium bicarbonate was given intravenously for every 5 units of blood. When the situation became urgent, type specific, uncrossmatched blood was given and in no instance was a reaction noted. Experience in using frozen blood was mentioned.

Postoperatively, all patients were followed closely in the recovery room until their vital signs were stable and they were fully reacted (except for certain neurosurgical cases when the return of consciousness was expected to be delayed). The more critically injured patients were transferred to the surgical intensive care unit.

EVIDENCE FOR A PHOSPHORUS—DEPLETION SYNDROME IN MAN

Myron Lotz, MD, et al., New Eng J Med 278(8):409-415, Feb 22, 1968.

Antacids can impair phosphorus absorption in man. The long-term results of such impaired absorption are not fully appreciated despite knowledge of the vital role of phosphorus in life processes and the serious results of its depletion in animals. To determine depletion in man, studies were performed in three normal subjects and three patients with parathyroid dysfunction during prolonged treatment with antacids.

It was found that a syndrome of phosphorus depletion characterized by hypophosphatemia, hypophosphaturia, increased gastrointestinal absorption of calcium, hypercalciuria, increased resorption of skeletal calcium and phosphorus, and debility, with anorexia, weakness, bone pain and malaise, can be produced by prolonged treatment with nonabsorbable antacids such as magnesium-aluminum hydroxides.

DIAGNOSIS, MEDICAL AND SURGICAL MANAGEMENT OF CORONARY INSUFFICIENCY

Albert A. Kattus, Jr., MD, et al., Ann Intern Med 69(1):115-136, July 1968.

Coronary artery injections of radio-opaque material into the vessels of autopsy hearts first disclosed that angina pectoris in most cases is due to extensive narrowing and occlusion of these vessels by atherosclerotic disease. These studies also showed that the development of coronary collateral anastomoses could compensate to a great extent for obstructions in the coronary arteries.

The electrocardiographic hallmark of myocardial hypoxia, ST segment depression, has provided a valuable diagnostic method that identifies the presence of coronary insufficiency when it accompanies either spontaneous or induced anginal pain. The two-step test is a useful diagnostic method, and treadmill testing with electrocardiogram (EKG) monitoring provides a quantitative measure of the severity of angina as well as evidence of adaptation in the coronary circulation.

Coronary arteriography discloses the extent of coronary obstructive disease, its accessibility for surgical correction, and the extent of compensatory collateral development. Surgical attempts at direct relief of coronary obstruction have been disappointing, but some brilliant successes point out the need for further study of this field. Control of serum lipid levels by diet and drugs offers hope of reducing the risk of coronary disease. A carefully graded walking exercise program may lead to improvement of clinical angina and treadmill performance in selected patients; this may provide a method for medical revascularization of the heart.

PULMONARY DISEASE OF VASCULAR ORIGIN

David E. Dines, MD FCCP, Dis Chest 54(1):3-12, July 1968.

The differential diagnosis of pulmonary disease of vascular origin must include pulmonary edema, uremia, Loeffler's syndrome, periarteritis nodosa, Wegener's granulomatosis, systemic lupus erythematosus, scleroderma, rheumatoid lung, pulmonary hemosiderosis, pulmonary purpura with nephritis, a pulmonary embolism and pulmonary arteriovenous fistula. Pulmonary edema and uremia have been included because of the roentgenographic features (pulmonary vascular congestion, pleural effusion, interlobar collections of fluid) which must be distinguished from those of other vascular disease that cause pulmonary parenchymal infiltrations.

DENTAL SECTION

HOW SAFE ARE X-RAYS?

Mike Michaelson, Today's Health, June 1968.

Bewildered by rumors, half truths and scare stories of radiation "hazards" an anxious public is asking: "How safe are X-rays?" The dental profession, too, is encountering, and is deeply concerned with this "X-ray fear syndrome."

Can a confused public be reassured that there is no cause for alarm, that X-ray examinations are safe?

Every citizen gets some radiation, even if he never visits a physician or dentist. He is exposed to "background radiation," which comes from cosmic rays, radioactivity in the earth, building materials, and even from food and body substances. A current estimate by the National Council on Radiation Protection and Measurements puts the average annual dose of background radiation per person at 120 millirads. (The "rad"—radiation-absorbed dose—is one commonly used index of measurement. A millirad is one thousandth of one rad.)

John W. Stanford, Ph.D., secretary of the American Dental Association Council on Dental Materials and Devices states, "A full mouth X-ray diagnosis involving 12 to 14 pictures would, when obtained by use of approved, modern techniques, expose a patient to about the same amount of radiation to the gonadal area as he would receive from background radiation by walking down the street."

Against these minimal risks, and reverting to a "hazard-versus-benefit" equation, are the overwhelming advantages of the dental X-ray, without which, says Doctor Stanford, "it would be absolutely impossible to conduct modern dental practice."

Lauriston S. Taylor, Sc.D., who is president of the National Council on Radiation Protection and Measurements, points out that there are no clear dividing lines between what may be termed "safe" and "unsafe" with regard to radiation and the human. There have been almost no clinical observations of the effects of radiation at the low levels generated by X-ray equipment, "because so far as we know there are no observable effects of these low doses of radiation on man." Probably the greatest amount of information we have, he said, and the most important piece of information that we have, is no information at all. Much of the current data comes from converting effects observed at high exposure levels to possible effects at low exposure levels and from the extrapolation of animal data to man—and both techniques are fraught with uncertainties.

R. H. Chamberlain, M.D., a member of the National Council on Radiation Protection, summarized his thoughts on the latest X-ray scare: "The real tragedy occurs when even a single person may be misled by a distortion of radiation hazards to refuse a needed diagnostic X-ray examination."

(Abstracted by: CDR Joseph J. Lawrence, Jr., DC USN.)

CORRELATED STUDY OF ORAL CYTOLOGY AND HISTOPATHOLOGY

G. Shklar, I. Meyer, E. Cataldo, and R. Taylor, Boston, Mass., Oral Surg 25(1):61-70, Jan 1968.

The diagnostic reliability of oral cytology as compared to the biopsy procedure was tested on 2,052 lesions of the oral mucosa in which the possibility of carcinoma could be considered in the differential diagnosis. A biopsy and cytologic smear was obtained from each of the 2,052 lesions and both were evaluated by two separate pathologists. Eighty-two histologically obvious carcinomas were found in this series. In 12 of these cases, the cytologic smears were negative, representing a false negative incidence of 14.6%. Three other cases were read as atypical rather than suspicious or suggestive. There was not a single case in which a positive smear revealed an initially histologically undetectable lesion. On the basis of these figures the reliability of the biopsy procedure in the diagnosis of oral cancer was 100% as compared to 85.4% for cytology. Cytologic smears were also negative in 21 cases of premalignant dysplasia which were readily diagnosed by biopsy and 18 cases of false positive cytologic findings were recorded.

(Abstracted by: CAPT George H. Green, DC USN.)

PERSONNEL AND PROFESSIONAL NOTES

DENTAL CARIES MANAGEMENT PROGRAM

A pilot program in the management of dental caries was initiated at Marine Corps Recruit Depot, Parris Island, South Carolina, June 5, 1968. Participating in the pilot program were representatives of the Dental Corps of the Army, Navy and Air Force. To establish the background rationale for the project, *Doctor Maury Massler devoted one afternoon to the presentation of his studies on Vital Pulp Therapy. This was further supported by lectures concerning Pulpal Response to Intermediate Restorative Materials by CAPT Seymour Hoffman, DC USN. CAPT Malcolm D. Jendresen, DC USAF, presented his studies concerning formulations of intermediate restorative materials.

The pilot program stresses the concept of vital

* Professor of Pedodontics, Assistant Dean for Postgraduate and Teacher Education, University of Illinois College of Dentistry, Chicago, Illinois 60612.

pulp therapy[1,2] and utilization of a new Intermediate Restorative Material (IRM).[3] IRM is a color-coded zinc oxide-eugenol polymethyl methacrylate filling material indicated for intermediate long-term treatment of restorable teeth.

Recent research findings show that IRM may be used in situations that require intermediate treatments for periods in excess of one year. IRM requires minimal cavity preparation and may be placed over **affected dentin* in the event that indirect pulp capping is desired. Color coding indicates that the following has been accomplished:

Red—Place only in vital posterior teeth with affected dentin remaining.

Blue—Place only in vital posterior teeth which have had all affected dentin removed.

Ivory—Place only in vital anterior teeth with affected dentin remaining or when time does not permit placement of silicate, etc.

The DD-722-1 of each patient treated in this program contains a BUMED information sheet which provides instructions concerning evaluation of the project as well as provisions for further treatment.

* The term *affected dentin* is used to identify dentin which has been demineralized but is not infected.

References

1. Massler, M. Preventive Endodontics: Vital Pulp Therapy. ***Dent Clin N Amer*** 663–673, November 1967.
2. Bender, I. and Seltzer, S. *The Dental Pulp* 111–112, Philadelphia, Lippincott, 1965.
3. Jendresen, M. D., Phillips, R. W., and Swartz, M. L. **A comparative study of four zinc oxide-eugenol formulations as restorative materials.** Presented at the 46th General Meeting of International Association of Dental Research, Hilton Hotel, San Francisco, California, March 20–23, 1968.

CANADIAN DENTAL OFFICERS VISIT NAVAL DENTAL SCHOOL

Twenty-one second lieutenants of the Royal Canadian Dental Corps, in the third phase of the Dental Officer Training Program at Base Borden, Ontario, Canada, visited the Naval Dental School, National Naval Medical Center, Bethesda, Maryland, on July 31, 1968.

This year marks the second in which officers from Base Borden have come to Washington to observe the operation of U.S. Federal dental services. In addition to the Naval Dental School, the week-long tour included visits to the Walter Reed Army Medical Center, National Institute of Dental Research, Armed Forces Institute of Pathology, and Army Medical Biomechanical Research Laboratory. The officers also visited the White House, Smithsonian Institution, and Canadian Embassy.

After a welcome from the Commanding Officer, CAPT W. C. Wohlfarth, Jr., DC USN, the group toured all departments of the Dental School Command. In the afternoon, the officers attended professional lectures presented by staff officers of the Dental School.

The Naval Dental School was included in the tour because the Royal Canadian Dental Corps and the U.S. Naval Dental Corps have maintained close liaison for many years. Since the 1940's nearly 100 Canadian dental officers have attended courses in residence at the School and about 35 are enrolled each year in professional correspondence courses.

MAJ James N. Wright, RCDC, was the conducting officer of the group. He is the Head, Department of Periodontics at RCDC School, Base Borden.

DENTAL HYGIENISTS AND DENTAL ASSISTANTS

To assist the Industrial Relations Officer in recruiting qualified dental hygienists and/or dental assistants, a current listing of accredited Dental Hygienists' Programs and Dental Assistants' Programs may be helpful. Listings may be obtained by request from their respective associations.

American Dental Hygienists' Association
Executive Secretary, Miss Margaret Swenson
211 East Chicago Avenue
Chicago, Illinois 60611

American Dental Assistants' Association
Executive Director, Mr. Louis J. Carow, III
211 East Chicago Avenue
Chicago, Illinois 60611

NURSE CORPS SECTION

RELATIONSHIP WITH THE FAMILY OF A CHILD WITH A MALIGNANT DISEASE

The "Relationship With the Family of a Child With a Malignant Disease" was presented by sister M. Luciana France, Director of Nursing, St. Jude's Children's Research Hospital, Memphis, Tennessee, to the nursing staff at the Naval Hospital, Memphis. The following are notes submitted by LCDR J. Ottoson, NC USN, Chairman, In-Service Committee, based on the subject.

Both personal experience and research relevant to the care of terminally ill children and their families was shared with the group. Because of the breath of the subject and research related to it, the emphasis was on the needs of the child and how these needs may be met.

The philosophy of this institution founded by Danny Thomas for the care of children with catastrophic illnesses is definitely family-centered. The Hospital provides for rooming-in and encourages parents to participate in the care of their children.

Focus is placed upon the behavior of these children, primarily in relation to their attitudes toward, and ways of dealing with their diseases. It is assumed that good physical care can and will be provided by most nurses; certainly, one excellent way to give psychological support is to provide meticulous physical care.

All children derive security from having consistent limits set for them. This is especially important to the sick child, who is likely to perceive his body as playing tricks on him; when one's own body becomes undependable, it is doubly important that his environment be consistently dependable. However, research has indicated that many parents, because of their own feelings of guilt and anxiety, attempt to satisfy the child's every wish and, in so doing, fail to establish a consistent environment.

Such a permissive attitude is intended to prevent frustration and provide for the most pleasant experience possible, if it is assumed the child has only weeks or months of life remaining. Unfortunately, what it frequently does is, to cause the child to regress to an excessively demanding and irritable state with desires which are instable. The parent who is already under stress reacts, at least inwardly, with irritation and hostility toward the child, and a vicious circle is established. The parents recognition of his own hostility contributes to his feelings of guilt, which in turn, lead to decreased limit-setting, increased demands by the child and greater efforts by the parent to satisfy these demands. Thus, ever greater feelings of frustration and hostility are produced in the parent. The child perceives this hostility and this provokes further feelings of insecurity which generate still greater demands.

This cycle is perpetuated as growing demands from the child kindle intensifying hostility in the parent. Ironically, the child may suffer more from the insecurity resulting from perceived parental hostility than he would from the frustration of being denied the fulfillment of a desire. The more normality that can be maintained, in terms of limit setting the more likely the child is to feel secure and, subsequently, the more content he will be.

Another aspect of normality emphasized at St. Jude is that parents are encouraged to keep their activities in the child's room as near normal as possible. They are asked to refrain from whispering and to express their feelings at times and places where the child will neither see nor hear them. They are also urged to spend part of each day away from the child so that they can release their tensions and many apprehensions and renew their strength for supporting him. Conferences about the child's condition are held outside the room.

How much information about the disease and its therapy is given to parents and children? At St. Jude, the parents are told everything about the disease and its treatment which they are able to understand and wish to know. The children are told by the medical and nursing staff only what they already know—that is, that they are bleeding, or that they are having bone pain and so on, depending upon their symptoms, age and desire for information. It is the parents function to decide what and how much to tell the child about his disease and his prognosis, and who should tell him. They may then delegate this task to a trusted friend; a minister, a doctor, a nurse, or other staff members.

Clinical observations have been made on how terminally ill children accept and react to their illness. Children do not usually become concerned with the idea of death, until they are about eight years old. This observation correlates well with what

has been documented through research: (1) that the "adult" concept of death as final and universal does not develop until approximately the age of nine; and (2) that the most common fear of terminally ill children over ten years of age, but not common in younger children, is fear of death.

Another study suggested that terminally ill, younger children need approximately the same kind of support as acutely ill children of the same age, since the fears of the terminally ill children studied corresponded very closely to those of acutely ill patients in the same age groups: (1) for leukemia children under five, the greatest fear was that of separation from mother; and (2) for leukemic children between five and nine, the greatest fears were those of procedures of mutilation.

An older child is more likely to be concerned with the idea of his death. Sometimes, he will ask whether or not he is going to die. This can be a most upsetting experience for nurses and parents alike. To avoid the question by ignoring it or by changing the subject, helps the child very little. The basic issue is not whether to talk to the child about his serious concerns, but how to talk to him. The most helpful response the adult can give, is to calmly encourage the child to talk by asking him such questions as "Why do you ask that?" "What makes you think you are going to die?" or, "Do you feel badly today?" The child may then reveal more specifically what is troubling him.

It may be that he is responding to some behavior he has observed, his mother's crying, for example. When the nurse is able to elicit such concrete information, she can frequently satisfy the child by such statements as: "It makes mothers very sad when their children can't go out and play," or "It hurts mothers too, when their children must have shots." If the child's concern persists, the nurse at St. Jude is likely to acknowledge to him verbally that he is very sick. It is, well to follow this statement with two further statements: (1) "The doctors and nurses are working very hard to help you feel better," and (2) "You have to help us get you back on your feet." At this time, a child may be given a specific task: "Try to drink lots of water." "Eat all of your lunch;" or, simply "Rest for a while now and try to sleep."

The rationale behind this approach is that the child already knows that he is very sick because of the way he feels and that to deny this reality merely convinces him that he has no one with whom he can talk. It is suggested that some acknowledgment of the disease to the child in terms of what he is experiencing is helpful in preventing him from feeling isolated.

The patient is not told that the doctors are working to make him well, for this would be an untruth and later the child would be likely to feel that we have betrayed his trust. Finally, the child is encouraged to become an active participant in his care in order to decrease his feelings of helplessness.

As older children become aware of how seriously ill they are, it is common for them to guess the nature of their disease even though everyone is certain they have been told nothing. The stricken child may have numerous clues that something terrible is happening to him. Children are extremely sensitive to the feelings of others, particularly to tension and anxiety in their mothers. The impact upon the mother when she is told that her child has leukemia, for example, is sufficient to let the child know that something is wrong.

In addition to the psychological implications of the disease, physical symptoms appear which tell him very emphatically that something is wrong. As though these two phenomena were not enough the child suddenly begins to make numerous visits to doctors in clinics and hospitals and to receive many painful and frightening procedures. Thus, there are many clues to tell the child that he is very ill. The older child who knows or suspects his diagnosis or prognosis needs an opportunity to discuss his future with someone. At St. Jude, teenage patients who know their diagnosis are invited to talk monthly with the social worker who encourages them to discuss their feelings and their plans for the future.

There are no easy answers to the questions which arise when caring for these patients. In the end, how the individual nurse deals with them must be very closely related to her religious beliefs, her philosophy of life, and her feelings about death. Nurses are urged to find someone with whom they can work through their emotional and psychological reactions about death, so that their energies can be freed to meet the needs of the children and their families.

RESEARCH SECTION

LIST OF RECENT PUBLICATIONS FROM RESEARCH LABORATORIES

The following papers have been completed by research activities under the direction of the Bureau of Medicine and Surgery.

Naval Aerospace Medical Institute:

"Diagnostic Criteria for Grading the Severity of Acute Motion Sickness," by Ashton Graybiel, Charles D. Wood, Earl F. Miller, and LT Dewey B. Cramer. *Aerospace Medicine* 39(5), May 1968.

"Expansion of the Naval Flight Officer Student Prediction System," by Richard F. Booth & Floyd E. Peterson, May 1968. Report: NAMI —1038.

"Relations Between Vestibular Nystagmus & Visual Performance," by Fred E. Guedry, Jr., Ph.D., *Aerospace Medicine* 39(6), June 1968.

"The Relationship of the Naval Aviator's Speech Discrimination Test to the Pure Tone Audiogram," by James W. Greene, April 9, 1968. Report: NAMI—1037.

"A Simple Method for Percutaneous Introduction of Cardiac Catheters," by Hassan H. Khalil, March 29, 1968. NAMI—1035.

Naval Medical Research Unit No. 2:

"Aquatic Snails as Intermediate Hosts for Angiostrongylus Cantonensis on Taiwan," by Ping-Kuo Chang, John H. Cross, and Steve S. S. Chen. *Journal of Parasitology* 54(1), February 1968.

"Down's Syndrome with G/G Translocation & Triple-X Syndrome in the Same Sibship," by Shih-Wen Huang and Irvin Emanuel. *Acta Paediatrica Sinica* 8(4), Oct-Dec 1967.

"The Filarial Parasite, Macacanema Formosana From the Taiwan Monkey and its Development in Various Arthropods," by John F. Bergner, Jr., Ph.D. & Leo A. Jachowski, Sc.D. *The Formosan Science* 22(1), 1968.

"Growth and Development of Rats in Relation to the Maternal Diet," by B. F. Chow, R. Sherwin, A. M. Hsueh, B. N. Blackwell, and R. W. Blackwell. *Journal of the Formosan Medical Association* 67(4), April 28, 1968.

"Hemoglobin G Taiwan-Ami," by R. Quentin Blackwell and Chen-Sheng Liu. *Biochemical and Biophysical Research Communications* 30(6), 1968.

"The Pathophysiology of Cholera," by J. W. Fresh, CDR MC USN. *Bulletin of Pathology*, May 1968.

"Studies of Immune Mechanisms in Leprosy," by Ward E. Bullock, LCDR MC USNR. *New England Journal of Medicine* 278, February 8, 1968.

Navy Medical Neuropsychiatric Research Unit:

"Autonomic Correlates of the Spontaneous K-Complex," by Laverne C. Johnson & Wayne K. Karpan. *Psychophysiology* 4(4), April 1968.

"A Mental Health Survey Instrument: the Health Opinion Survey," by E. K. Gunderson, Ph.D., Ransom J. Arthur, CDR MC USN & Walter Wilkins, Ph.D. *Military Medicine* 33(4), April 1968.

Naval Medical Research Institute:

"Use of Intraosseous Metal Appliances in Fixation of Mandibular Fractures," by Eugene J. Messer, DDS, Daniel E. Hayes, DDS, and Philip J. Boyne, DMD MS. *Journal of Oral Surgery* 25, November 1967.

Naval Radiological Defense Laboratory:

"Early Alveolar Cell Mitotic Activity and Pulmonary Tumor Incidence in Urethan Treated X-Irradiated Mice," by T. R. Birdwell, LCDR MC USN and L. J. Cole. 12 April 1968. NRDL Technical Report 68-51.

"Ontogeny of the Mouse Immune System," by M. L. Tyan and L. A. Herzenberg. May 14, 1968. NRDL Technical Report 68-57.

Naval Submarine Medical Center:

"Computation of Continuous Decompression Schedules for Deep Sea Dives," by James S. Robertson and George Moeller. March 19, 1968. Report: NSMC #517.

"Emergency Dental Treatments by Medical Officers on Isolated Duty," by William R. Schiller, CDR DC USN, February 28, 1968. Report: NSMC #513.

"Pulmonary Functions During Saturation-Excursion Dives Breathing Air," by James H. Dougherty, Jr., and Karl E. Schaefer. *Aerospace Medicine* 39(3), March 1968.

"Stereoscopic Acuity Underwater," by Saul M. Luria, Ph.D., February 27, 1968. Report: NSMC #510.

Naval Unit, Fort Detrick:

"Immunofluorescence, an Annotated Bibliography III. Studies of Fungi, Metazoa, Protozoa, and Rickettsiae," by Warren R. Sanborn. March 1968. Misc. Pub. #20.

OCCUPATIONAL MEDICINE SECTION

A METHANOL POISONING OUTBREAK IN KENTUCKY

A CLINICAL EPIDEMIOLOGIC STUDY

R. L. Kane, MD; W. Talbert, MD; J. Harlan, MD; G. Sizemore, MD, and S. Cataland, MD, Lexington, Ky, Arch Environ Health 17(1):119-129, July 1968.

A change in the brand of shellac thinner used to make an alcoholic beverage resulted in six deaths from methanol poisoning. In screening all potentially poisoned persons available with serum methanol, ethanol, pH, and electrolyte determinations, many asymptomatic methanol poisonings were discovered. A correlation was established between severity of illness and level of ethanol, further suggesting a protective effect.

Among different types of treatment used with the 12 hospitalized cases peritoneal dialysis was shown to be effective, with a clearance rate five to ten times that obtained with forced fluid diuresis.

Several epidemics of methanol poisoning have been described in the medical literature. It is our purpose to describe a group of cases resulting from a common-source epidemic which involved 18 people, of whom eight died. Of the 18 known cases, 11 were treated at the University of Kentucky Medical Center with only one death despite several patients with methanol concentrations of 200 mg or more per 100 ml blood. Fatalities have been reported with serum methanol levels of under 200 mg/100 cc. In addition to providing treatment, the hospital instituted an emergency screening program for all suspected methanol imbibers. This procedure facilitated the detection and treatment of asymptomatic persons with markedly elevated blood methanol levels, which added a new dimension to the clinical experience with methanol poisoning. Frequent chemical determinations provided new information on the rate of methanol excretion by various routes and the relative efficacy of different modalities of therapy.

Since Bennett's work in the epidemic of methanol poisoning in Atlanta in 1953, the major therapeutic advance in the treatment of methanol poisoning has been the application of dialysis therapy with special attention focused on extracorporeal treatment. In none of the 11 patients studied here was hemodialysis used. Peritoneal dialysis was evaluated and attempts were made to follow methanol excretion rates with and without dialysis.

Epidemiology

The epidemic began with the distribution of diluted paint thinner from a regular source in a low socioeconomic area of Lexington. "Heads" is an alcohol drink made by diluting shellac thinner, usually a brand with a high ethanol and low methanol content. On this occasion a different compound was employed —a shellac solvent (Thinz-all) with approximately 74 vol% methanol. Analysis of fluid contained in bottles found near some of the victims showed that the solvent probably had been diluted to a final concentration of about 37 vol% methanol. Two major population groups appear to have been affected: (1) the Negroes living in the neighborhood of the seller; and (2) the white derelict alcoholics who relied on this seller for their regular supply.

Shellac thinner can be purchased commercially at any paint store for approximately $1.95 a gallon. When this is diluted one or two times (often to the purchaser's taste) it is usually poured into old half-pint bottles which sell as "heads" for approximately 25 cents. The potential profit thus ranges from 100% to 200%.

Reconstructing the events surrounding this particular episode, apparently two or three gallons of thinner were purchased and diluted once with water. About half of the liquor so obtained was served as the major refreshment for a party held at an adjoining house. Part of the remaining lot was sold along the usual channels until the seller himself became ill. At this point his wife took over the business and continued to distribute the methanol although it had been suspected to be "a bad batch." There was no reliable means of determining how many persons had obtained some of this alcohol.

The initial patient (case 11) was admitted to the University of Kentucky Medical Center with a history of drinking denatured alcohol. He became comatose shortly after admission and never regained consciousness. By the following morning reports of several deaths at neighboring hospitals and the finding of a corpse surrounded by empty bottles containing traces of methanol indicated that an epidemic of methanol poisoning might be developing. The police

identified the distributor when, after his death, his wife presented herself in our emergency room as a possible victim of the poison within 24 hours of the first death. Although she refused admission after learning that she had no methanol in her blood, she offered us a list of names of persons to whom she claimed to have sold the "heads." The newspapers and mass media publicized the story and many people referred themselves to the emergency room for screening. The police searched the known haunts of alcoholics and brought in more suspected imbibers for investigation. The area where the alcohol had been made was visited by one of the authors (R. K.) after the admission of the second case, and several additional victims identified themselves for treatment at that time.

In all, some 26 persons were screened in the emergency room of whom 13 were admitted, 11 for methanol intoxication. The screening procedure in the emergency room was based on immediate determinations of electrolytes and venous pH, with blood methanol levels reported within 12 hours. On the basis of clinical examination and acid-base status all suspects were either admitted, held in the emergency room or held by the police until the report of blood methanol levels was available.

It was not possible to ascertain reliably the association of any of those screened to the source of methanol. Several of those seen in the emergency room had referred themselves for drinking "bad heads" but this proved to be isopropyl alcohol or ethanol.

Once the patients had been convinced that our laboratory studies indicated serious potential illness and possible death, they agreed to hospitalization but were not universally cooperative. Over half the patients left against hospital advice during the recuperative phase of their illness and several refused to permit various procedures. We had hoped to follow these patients after discharge, but they neither returned for further care nor could they be located at the addresses given. Many of our patients were chronic alcoholics with no fixed address.

Results

Of the 11 persons with significant blood methanol levels (greater than 30 mg/100 cc), all but the original patient were alert and oriented on admission. In general all patients were given sodium bicarbonate ($NaHCO_3$), as needed, either orally or intravenously, to maintain normal serum pH. Force fluid regimens were used throughout with inputs of 6 to 8 liters a day for each patient. Ethanol therapy was attempted but proved unsuccessful. Initially three patients were treated with peritoneal dialysis; a fourth patient was begun on dialysis after more conservative therapy was unsuccessful. The dialysate of one patient was analyzed for methanol content. One pair of patients with approximately equal methanol and ethanol levels, both asymptomatic, can be used, in retrospect, to appreciate the clinical and laboratory improvement with and without dialysis. However, as complications ensued in the patient on the diuresis regimen, he too was begun on dialysis with substantial improvement. In several instances vitamin A was given as recommended by Tonning et al.

Urine samples and gastric drainage were collected from those patients on forced fluid and dialysis regimens in an effort to assess clearance rates by these routes. Liver function tests, amylase values, and glucose levels were obtained on most of the patients. A lumbar puncture was performed on nine patients within one to six hours after admission as soon as it was feasible (two patients refused this procedure). In addition to the standard measurements of cell count, total serum protein, and glucose, this fluid was also analyzed for methanol and ethanol.

Seven persons outside the medical center died in connection with the epidemic. Of these, two were autopsied and in all but two cases (ironically, one was the dispenser of this poison) blood was obtained for methanol levels. These unconfirmed cases were included because of their strong historical connection with the source of the methanol. Unfortunately one had been embalmed which prevented toxicological analysis. The other had been found amidst a number of empty bottles which later analysis confirmed were "heads."

It was originally hoped that the patients might provide some insight into the amount of methanol each had consumed. However, on repeated questioning, they gave markedly varied responses which showed little trace of reliability. Furthermore, a few denied drinking any "heads" at all until methanol had been proven to be present in their blood, emphasizing the danger of screening the asymptomatic patient in an epidemic on the basis of history alone or in conjunction with pH and bicarbonate determinations. All did at some time admit to obtaining their "heads" from the same general area but most were reluctant to implicate any particular source.

Conclusions

Although peritoneal dialysis is not as rapid as hemodialysis in removing methanol and its toxic products, it is much more available to the practic-

ing physician in virtually any medical institution. With the technical advances in clinical toxicology it is now possible to obtain blood methanol determinations rapidly, thus enabling the clinician to assess the patient's present condition and prognosis in light of acid-base status and methanol levels. Many instances like those described may be found which will add a new dimension to our understanding of methanol poisoning, namely the clinically asymptomatic case which will readily respond to peritoneal dialysis.

We feel that several of the patients described in this report represent a new syndrome in the lore of methanol poisoning—specifically, asymptomatic persons with high serum levels of methanol who have been discovered and treated before the terrible effects of the poison could become manifest. As more of these epidemics are described at a time when technical developments make possible rapid blood methanol determinations, more of the answers to the mysteries of the human form of this very species of specific disease may become clear.

We would recommend that future investigators consider the use of compounds such as Tris-buffer or urea, which may serve a dual role either as a buffer-binder or diuretic-binder, respectively. Utilizing modern laboratory facilities, detailed analyses of patients' urine may yield valuable information about methanol metabolism.

THE INHALATION TOXICITY OF PYROLYSIS PRODUCTS OF POLYTETRAFLUOROETHYLENE HEATED BELOW 500 DEGREES CENTIGRADE

R. S. Waritz, PhD and B. K. Kwon, Wilmington, Del,
Amer Industr Hyg Ass J 29(1):19-26, Jan-Feb 1968.

Quantitative evidence has been obtained which indicates that the principal toxic component in the pyrolysate from PTFE (Teflon[R]5) at the first temperature at which rat mortality is observed (Approximate Lethal Temperature, ALT), is a particulate material which may have other toxicants adsorbed on it. The toxicity of this particulate varies, depending upon the conditions under which it is generated. At 30°C above the ALT, perfluoroisobutylene could be the principal toxic agent. The data correlate well with known chemical reactions as well as observations and hypotheses of other investigators.

Introduction

Polytetrafluoroethylene (PTFE) (Teflon[R]5) has had widespread utilization and interest because of its desirable combination of plasticity, lubricity, chemical inertness, low toxicity and thermal stability. This combination of properties is unmatched in any other organic, inorganic, synthetic, or naturally occurring polymer. Because of its thermal stability, many of the uses of PTFE have been at elevated temperatures. Consequently, the toxicity of PTFE at elevated temperatures has been the subject of several toxicological investigations. These investigations have disclosed that, as with other synthetic and naturally occurring polymers, PTFE does evolve toxic materials when heated above certain temperatures.

The first indication of the evolution of toxic materials from PTFE at elevated temperatures came during the development of molding technology for this polymer. It was observed that proximity to PTFE at sintering temperatures (ca. 350°C) could result in a temporary influenza-like illness. It apparently resulted from inhalation of some material evolved from the heated polymer. The symptoms were similar to those of the already well known "metal fume fever." This condition, when caused by PTFE fumes, was subsequently named "polymer fume fever." The etiologic agent for polymer fume fever has not yet been identified, although it has been suggested that it is a particulate material.

In 1954, Treon et al. reported that the pyrolysis products evolved from PTFE at 375°C in air were toxic for several animal species by inhalation. They identified octafluoroisobutylene (PFIB) and oxygen difluoride in the pyrolysis products by infrared absorption spectra. They reported no quantitative measurements of the amounts of these materials present. In 1955, Zapp et al. reported that products lethal to rats were evolved from PTFE heated at 300°C in an air atmosphere. Tetrafluoroethylene (TFE), hexafluoroethane, hexafluoropropylene

(HEP), octafluorocyclobutane (OFCB), and PFIB were qualitatively identified in the pyrolysate by infrared absorption spectrophotometric methods. They also reported that PFIB was almost ten times as toxic to rats by inhalation as phosgene; a six-hour exposure to 0.5 ppm of PFIB being lethal. Additional studies were reported by Clayton et al. in 1959. These studies indicated that some PTFE resins could be heated to 350°C in air without the evolution of materials lethal to rats. They also indicated that at 300°C in air, PTFE or its pyrolysis products reacted with glass resulting in a somewhat enhanced toxicity. Clayton et al. also reported that filtration of the pyrolysis stream through a Millipore[R] filter of 0.45 μ pore size ameliorated the toxicity of the pyrolysis products. These studies and those of Zapp et al. were the first indication that a particulate material was implicated in the toxicity of PTFE pyrolysis products at certain temperatures.

Subsequently, the acute inhalation toxicity of the remainder of the identified gaseous pyrolysis products was studied. The respective Approximate Lethal Concentrations (ALC) for rats for a four-hour exposure to TFE or HFP were found to be 40,000 ppm and 2500-2800 ppm, respectively. An atmosphere of 80% hexafluoroethane and 20% oxygen or 80% OFCB and 20% oxygen was not lethal to rats by inhalation during a four-hour exposure.

The analytical methods available at the time of these earlier studies were unsuited for reliable quantitative analysis of the small amounts of gaseous materials evolved at the lethal temperatures. For this reason, it also was not possible to determine if these gases were present in lethal concentrations at the pyrolysis temperatures or if filtration removed any gaseous components in addition to particulate material from the PTFE pyrolysate stream. It was not until the advent of gas chromatography that it became possible to reliably identify and quantitate the trace amounts of gaseous materials present at the first temperature at which products lethal to rats (Approximate Lethal Temperature, ALT) were evolved from PTFE.

This paper describes the results of toxicological studies on the pyrolysis products of one type of PTFE utilizing gas chromatographic techniques for identification and quantitation of the gaseous pyrolysis products.

Discussion and Conclusions

The data presented in this paper confirm the earlier qualitative results of Zapp et al. and Clayton et al. which indicated that at the ALT, the principal toxic agent evolved during the pyrolysis of PTFE was a particulate material.

The present studies, when interpreted with the background of toxicological information developed since the earlier studies of Zapp and Clayton, showed that there were toxicologically insignificant amounts of TFE, HFP, PFIB or hydrolyzable-fluoride-containing materials evolved from PTFE at the ALT. The present studies also showed directly, that filtration of the pyrolysis stream at the ALT did not significantly reduce the concentration of any of these components in the pyrolysate but did remove the toxic factor. Filtration must have removed the toxic factor by filtration rather than chemical reaction with the filter material, since three chemically different types of filters performed identically.

The data also indicate, as might be expected, that the toxicological characteristics of the particulate, and the amount formed, depend upon the oven atmosphere. It is also likely that the physical, chemical and toxicological properties of the particulate will change with the temperature at which it is generated. We have not, as yet, carried out any experiments bearing on the chemical complexity of particulate. It may be a fluorocarbon matrix with adsorbed toxicants and more toxic than any of its components. Alternatively, it may be a fluorocarbon matrix with a high toxicity due solely to its particular physical and chemical properties. Some characterization work has been carried out on particulate with the Du Pont Company, but the characterization is not yet complete.

Although the toxicity of the particulate generated under a nitrogen atmosphere is not surprising, it is possible that it would have had even lower toxicity had all oxygen been rigorously removed from the nitrogen. If so, this would have important industrial hygiene ramifications, since it would then be possible to use PTFE at higher temperatures if an inert atmosphere were provided in the immediate vicinity of the heated PTFE fabrication. This aspect will be studied further.

These studies and those of Scheel et al. have also developed a toxicologically important relationship between the pyrolysis temperature and the principal toxicant from PTFE. Particulate, whatever its chemical composition, is the principal toxic agent at the ALT in air. However, at temperatures 25°C above the ALT, PFIB is formed and, at temperature 30°C above the ALT, it is present in lethal concentrations. At temperatures 100 to 300°C above the ALT, carbonyl fluoride is probably the principal toxicant.

The relative abundance of the respective toxicants at various temperatures is, of course, a function of the reaction kinetics for the various reactions involved. Thus, their abundance over particular temperature ranges will depend upon the decomposition temperature of the PTFE. For example, a PTFE that did not decompose until 600°C would probably decompose almost exclusively to carbonyl fluoride in an atmosphere containing oxygen.

A strictly analogous toxicological situation pertains in the case of the pyrolysis of hydrocarbons in air. Their toxicity at room temperature is due solely to the toxicity of the particular hydrocarbon molecule. As the temperature is raised, thermal "cracking" and rearrangement occurs and the toxicity of these products becomes important. As the temperature is increased further, carbon monoxide is formed and its toxicity usually dominates. With further increases in temperature, carbon dioxide is formed and its toxicity is predominant. Thus, here also, the toxicological determinant depends upon the temperature of the system.

The first step is a random homolytic chain cleavage which requires heat and probably does not require oxygen. The short chain represents the primary particulate. A rearrangement product of this primary particulate is probably the prevailing particulate when nitrogen is the furnace gas.

The terminal $-CF_2-CF_2$ bond which results from the cleavage has an energy of 30-40 kcal less than the internal $-CF_2-CF_2$ bonds according to Errede. Thus, difluorocarbene would tend to form preferentially from this fragment, although the evidence indicates that in the absence of oxygen it can also rearrange to give a stable molecule. In the absence of oxygen, the carbene moieties would tend to combine to form TFE. When sufficient TFE accumulated, a carbene would stand a good statistical chance of reacting with TFE, instead of another carbene, thus forming HFP. Then as HFP built up, the difluorocarbene radicals could also react with it to form PFIB and/or normal perfluorobut-2-ene. This build-up could continue to higher molecular weight compounds, depending upon conditions. Octafluorocyclobutane, which has been found under certain conditions, could be formed by the dimerization of TFE.

In the presence of air (oxygen) competing reactions are possible, as indicated. The primary particulate end groups can react with O_2 to form a second type of particulate with carboxylic acid fluoride end groups. We believe that this secondary particulate is the highly toxic form. These acid fluorides can also hydrolyze to give carboxylic acids and hydrofluoric acid. The difluorocarbene can also react with O_2 as shown to form carbonyl fluoride. The rates of all oxidative reactions would increase with temperature, as mentioned above, until, as Scheel et al. have shown, at ca. 550°C, the polymer backbone and all fragments are oxidized to carbonyl fluoride.

This hypothesis explains the large increase in TFE and HFP that was observed with a nitrogen cover gas, and explains why TFE was the first to appear in the pyrolysate, followed by HFP and PFIB.

This theory also accounts more readily for the presence of HFP and PFIB in the pyrolysate, than the former theory of PTFE degradation where it was postulated that the primary reaction was the abscission of the 2C fragment, TFE. HFP, being a three carbon molecule, could not be readily explained by the old hypothesis, since it is difficult to get a three carbon fragment by building up two carbon fragments unless cleavage of six carbon fragment or something even more exotic is postulated. It is also difficult to explain the branched chain PFIB on the basis of build-up by two carbon fragments unless cleavage of a branched six or eight carbon chain occurred. The present hypothesis also explains the high chamber acidity and higher hydrolyzable fluoride, even with filtration, when air is the oven gas, since carbonyl fluoride, hydrogen fluoride, and low molecular weight acid fluorides could easily pass through the filter.

The earlier work of Zapp et al. and Clayton et al. indicated that the ALT for high molecular weight PTFE was higher than that of low molecular weight PTFE. This was the first indication of toxicological differences between different types of PTFE. Since several types of PTFE are made by the various manufacturers, it is imperative to specify as completely as possible the PTFE used in pyrolysis studies. In the absence of more definitive specifications, it may be necessary to use trade names in describing samples used for testing and to rely on the integrity of the manufacturer to maintain the identity of a type of PTFE sold under a particular trade name.

OCCUPATIONAL AND THERAPEUTIC RADIATION EXPOSURE PROBLEMS

RADM F. B. Voris, MC USN,
CAPT B. K. Hastings, MC USN,
and CDR C. F. Tedford, MSC USN.

At the Navy's request, representatives of the Bureau of Medicine and Surgery, the Atomic Energy Commission, Bethesda Naval Hospital, and Naval Ship Systems Command met informally with the Executive Director of the Federal Radiation Council to consider occupational radiation exposure problems. This meeting was held to determine a method of developing information, guidance, and assistance in establishing criteria and standards on the limits of occupational radiation to which Navy military personnel and civilian employees may be safety exposed when the personnel involved have previously received radiation exposure through medical and/or dental therapeutic procedures.

The representatives attending this meeting agreed that the Navy should inform the Secretary of Defense of the problem in order that he consider the problem as one of all the services and not unique to the Navy.

The Secretary of Defense in turn requested that the Federal Radiation Council determine appropriate guidelines to assist the Armed Services in establishing acceptable standards concerning occupational radiation exposure of civilian employees and servicemen who have previously received therapeutic or diagnostic radiation exposure.

The Federal Radiation Council has requested the National Academy of Sciences to make a study of the problem and to make recommendations on total allowable radiation exposures. Should definitive regulations be devised, they would apply equally to all governmental agencies and thus they must necessarily be reviewed by the Department of Justice and approved by the President.

Until such standards have been promulgated, the Navy has found it necessary to develop a method of obtaining and evaluating therapeutic medical radiation exposure information from candidates or workers who are involved in radiation fields. For this purpose the Surgeon General has established a Medical Advisory Board to evaluate therapeutic radiation exposure as it relates to employment in radiation hazard areas. The Board will determine the eligibility of individuals whose records it reviews to begin or continue to work in an industrial radiation environment. These records shall be forwarded to the Medical Advisory Board via the Bureau of Medicine and Surgery, Code 74, for appropriate action. They shall include: (1) completed current reports of medical examinations, Standard Form 88; (2) report of medical history, Standard Form 89; (3) a case history of therapeutic exposures denoting types and amounts or intelligent estimates of amounts of exposures; and (4) a completed record of occupational exposure to ionizing radiation, DD Form 1141.

A forthcoming revision of Chapter II of NAVMED P-5055, "The Radiation Health Protection Manual," will formalize the above information required to carry out these procedures.

The screening and evaluation of Navy military personnel and civilian employees who have previously received medical and dental therapeutic radiation exposure will afford them a greater degree of personnel protection and safety.

EDITOR'S SECTION

PHOTOSENSITIVITY TO SYSTEMIC AND TOPICAL DRUGS

Med Lett Drugs Ther 10(8):
32, Apr 19, 1968.

Among the numerous systemic drugs known to cause photosensitivity reactions are the sulfonamides (antibacterial, thiazide, and hypoglycemic), tetracyclines, especially demethylchlortetracycline (Declomycin), griseofulvin (Grisactin; Grifulvin V; Fulvicin-U/F), and some phenothiazines, barbiturates and salicylates (Medical Letter, Vol. 7, p. 38, 1965). Other commonly used systemic drugs recently reported to cause photosensitivity reactions include oral contraceptives (L. R. Erickson and E. S. Peterka, JAMA, 203:980, March 11, 1968), and quinethazone (Hydromox) (R. C. Miller and V. S. Beltrani, Arch. Derm., 93:346, 1966).

Topical Drugs—The topical agents most frequently responsible for photosensitivity reactions are the halogenated salicylanilides (L. C. Harber et al., Arch. Derm., 96:646, 1967). These antiseptic agents are present in Cuticura, Lifebuoy, Phase III, Safeguard, Zest and other soaps. Photosensitivity recations may also occur with other antiseptics contained in deodorant soaps and other products, including bithionol and less frequently carbanilides and hexachlorophene (J. H. Epstein et al., Arch. Derm., 97:236, March 1968). Bithionol is present in some cosmetics and until recently was used in

first-aid creams, acne preparations, soaps, and other toilet preparations. The Food and Drug Administration plans to stop the use of bithionol in cosmetic products, and has already barred its use in other toilet preparations and in prescription products. Other cosmetic preparations, including those containing bergamot or citron oils, are also capable of causing photosensitivity reactions.

Treatment—Photosensitivity reactions are usually characterized by erythematous, vesicular, papular or eczematous lesions. The reaction may persist for prolonged periods without further contact with the sensitizing agent. The primary therapy is elimination of the photosensitizing agent or restriction of exposure to sunlight. If exposure is unavoidable, a topical sunscreen preparation should be used. Erythematous and vesicular reactions can be treated like ordinary sunburn, with cold water compresses or cool baths. For severe reactions, corticosteroids may be needed. Photosensitivity reactions sometimes persist and require treatment for many months; for persistent reactions some Medical Letter consultants recommend, in addition to steroids, oral psoralens in doses of 10 to 20 mg daily for several weeks, with controlled exposure to ultraviolet light or sunlight.

(For a recent review of cutaneous reactions to drugs, see R. L. Baer and H. Harris, JAMA, 202: 710, November 20, 1967.)

CHEMICAL, BIOLOGICAL AND RADIOLOGICAL WEAPONS ORIENTATION COURSE

The Chemical, Biological, Radiological Weapons Orientation course will be conducted at the U.S. Army Chemical Corps Proving Ground, Dugway Proving Ground, Dugway, Utah, by the Department of the Army during fiscal year 1969. The duration of the course is three and one-half days.

Officers of the rank of Lieutenant Commander or above are eligible to attend. Civilians in the grade of GS-12 or higher must be in a key position where need-to-know is mandatory. Officers of the rank of Lieutenant and civilians in the grade of GS-11 may be granted waivers where special circumstances warrant their attending the course. All requests for waivers must be accompanied by job description and need-to-know certification. Persons who have received complete CBR briefings during the past two years should consider delaying their attendance. Security clearance of INTERIM TOP SECRET is required. Limited quotas will be provided the Bureau of Medicine and Surgery by the Chief of Naval Personnel on a "first come first serve" basis. Requests should be forwarded in accordance with BUMED-INST 1520.8 Series.

The course provides a high level orientation on Chemical and Biological Warfare, and Radiological Implications of Nuclear Warfare, and is designed to acquaint military and civilian personnel of the Armed Forces with United States doctrine, policy, techniques and capabilities in CBR Warfare.

Convening Dates of Courses

4	Nov	1968	31	Mar	1969
18	Nov	1968	14	Apr	1969
2	Dec	1968	21	Apr	1969
9	Dec	1968	28	Apr	1969
24	Feb	1969	12	May	1969
3	Mar	1969	19	May	1969
10	Mar	1969	2	Jun	1969
24	Mar	1969	9	Jun	1969

—Training Branch, BuMed.

ANESTHESIA SUPPORT PROGRAM EXPANDED

The Anesthesia Support Program is a system of training whereby physicians receive approximately 11 months of instruction in basic anesthesia techniques, inhalation therapy, proper use of narcotic analgesics, sedatives, hypnotics and antiemetics, management of the comatose patient, management of hypotensive states, rationale and experience in the use of vasopressors, as well as the pre-and post-anesthesia care of patients.

The program for FY 1969 was filled; however, the Bureau Professional Advisory Board has recently approved an expansion of the program at the Naval Hospital, Portsmouth, Virginia. This program is exempt from the customary "pay back" time requirement. Interested personnel should submit application through the chain of command to the Chief, Bureau of Medicine and Surgery (Code 316), Department of the Navy, Washington, D.C. 20390, as soon as possible.

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